Appendix 1: Technical Report

1.0 Introduction

The APA commissioned an evidence-based guideline on acute pain in children in 2005. The chairman was appointed, and a committee assembled representing a number of professional groups involved in children's pain management in the UK, see section 1 for names of committee members and the professional and patient groups they represent. The Association was not involved in the editorial process of the guideline itself except as represented by relevant committee members.

An initial meeting was held iat which existing published guidelines on paediatric acute pain were reviewed and the need for a guideline was discussed.

Published guidelines were appraised using the AGREE instrument (available at: http://www.agreecollaboration.org/1/agreeguide/sign/index.html), table 1. Although there are a number of guidelines concerned with paediatric pain, none of them covered all aspects that are included in the present guideline either in sufficient detail, or using comparable methodology. The committee therefore decided that the present guideline would add to the available information on the subject.

A basic structure of the guideline was agreed: incorporating the views of committee members and the bodies they represent. It was decided that the guideline should include advice on pain assessment, the management of painful medical and surgical procedures and a synopsis of analgesia and management strategies. The list of procedures included in the guideline were chosen by the committee, using their expert knowledge, on the basis of their perceived clinical frequency and importance. Following initial searches the list of procedures was revised according to the availability of research evidence.

2.0 Searches

Systematic methods were used to search for studies relevant to the three evidence-based sections of the guideline:

Section 3.0 Pain Assessment
Section 4.0 Medical Procedures
Section 5.0 Postoperative Pain

Members of the committee took responsibility for searches and appraisal of different parts of the guideline according to their area of expertise. Committee members worked in pairs in order to compile and check searches, they also

consulted with the other committee members and the chairman as and when necessary.

The published literature for the 10 year period 1996- 2006 was searched for studies, including meta-analyses and systematic reviews, evaluating the *effectiveness* or *validity* of pain management strategies or assessment methods including individual assessment tools for acute postoperative and procedural pain in children.

Bibliography reviews of review articles and published guidelines were also conducted in order to confirm that searches had identified all relevant publications.

Search strategies
Searches were limited to human studies, in English, in children 0-18 years old between the dates 1st January 1996- 31st December 2006. Databases consulted were Pubmed/Medline, Ovid, Cinahl, Embase, Psychlit, Ingenta, Web of Science, British Nursing Index and Cochrane Library.

General searches were performed using key word identifiers and key phrases: e.g. adolescent, child, children, pediatric, paediatric, neonate, preterm, infant, baby, analgesia, analgesic, acute pain, procedural pain, postoperative pain. These general searches were then further refined by searching key words and phrases specific to each section of the guideline i.e. pain assessment tools, procedural pain or postoperative pain, examples of key words are given in table 2, a full list of all key words is available on request from the editor. Manual searches of the bibliographies of review articles and other published guidelines were also performed in order to identify studies not obtained by electronic searches.

3.0 Study Selection and Data Extraction

Abstracts of studies that were identified in the searches were appraised for inclusion or exclusion by a member of the committee responsible for each section. If it was not possible to ascertain if a study met inclusion criteria from the abstract, the full article was obtained. In cases of uncertainty, the relevant study was discussed with the editor, or by the committee as a group in order to reach a decision. Inclusion and exclusion criteria for studies in each section of the guideline are given in table 3.

4.0 Study Evaluation, direct and indirect evidence

Included studies were evaluated for methodological quality using criteria shown below, and assigned the appropriate evidence level:

Level 1
1++
High quality Meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

1+
Well conducted Meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 -
Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

Level 2
2++
High quality systematic reviews of case-control or cohort studies. High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
2+
Well-conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2 -
Case control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal

Level 3
Non-analytic studies, e.g. case reports, case series

Level 4
Expert opinion

The quality of studies was assessed with the assistance of 'methodology checklists' for specific study types published by the Scottish Intercollegiate Guideline Network (SIGN) and available at:
http://www.sign.ac.uk/methodology/index.html

Assessment of bias was assisted by the use of the 'Oxford Bias Guide' and advice on evaluation of bias in clinical trials published in Bandolier Extra 2001 available at: http://www.jr2.ox.ac.uk:80/Bandolier/Extraforbando/Bias.pdf

Studies were summarised in data extraction tables, grouped according to subject and procedure, these are shown in appendix 4. A brief discussion of the available evidence for each procedure is included in each subsection under the heading 'evidence', a table is included that summarises the level of evidence available for the effectiveness of each analgesic strategy as listed

Direct evidence
Studies in children directly applicable to the age and procedure(s) as stated.

Indirect evidence
Evidence from studies considered by the committee to be sufficiently similar to the procedure in question to allow tentative extrapolation.

5.0 Grading and Formulation of Recommendations

Evidence was translated into recommendations for clinical implementation; they are presented at the start of each sub-section and summarised in Section 2.0. Recommendations were graded according to the level of evidence used to compile them, as shown below, and the relevant studies are directly cited with each recommendation. Indirect evidence was not included when recommendations were formulated or graded. Recommendations are listed in order of the strength of evidence currently available NOT according to their clinical importance or other criterion.

Grade A
At least one Meta analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or
A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

Grade B
Evidence including studies rated as 2++ or better, directly applicable to the target population, and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 1+ or 1++

Grade C
Evidence including studies rated as 2+ or better, directly applicable to the target population and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 2++

Grade D
Evidence level 3 or 4; or
Extrapolated evidence from studies rated as 2+

6.0 Good Practice Points

Indicate best clinical practice, based on the clinical experience and opinion of the guideline development group; they are provided in situations where published evidence was insufficient to make a formal recommendation, but the committee wished to emphasise important aspects of good practice.

7.0 Peer Review and Consultation

A draft of the guideline was made available for peer review and professional consultation between September and November 2007. Copies were sent to professional organisations represented by members of the committee and were made available on websites of the Association of Paediatric Anaesthetists and Royal College of Anaesthetists. Written feedback was obtained from the British Pain Society, the Royal College of Paediatrics and

Child Health and the Royal College of Nursing. Written comments were also received from 12 individuals. The guideline was officially endorsed by the Council of the British Pain Society at their meeting on 6th September 2007.

8.0 Conflict of Interest

No conflict of interest was declared by members of the committee.

Table 1: Existing Guidelines

Year	Title	Source	AGREE compliant
1999	The recognition and assessment of acute pain in children	RCN (UK)	Yes
2001	The recognition and assessment of acute pain in children	RCPCH (UK)	Yes
2001	Policy Statement: Assessment and Management of Acute Pain in Infants Children and Adolescents	AAP (American Academy of Pediatrics) APS (American Pain Society)	No
2004	Guideline for the Management of Pain in Children	British Association of Emergency Medicine	No
2005	Guideline Statement: the management of procedure-related pain in neonates	RACP (Australia) Paediatrics and Child Health Division	No
2005	Guideline Statement: management of procedure related pain in children and adolescents	RACP (Australia) Paediatrics and Child Health Division	No
2005	Acute Pain Management: Scientific Evidence*	ANZCA (Australia)	Yes

*adults and children

Table 2: Examples of Key Words and phrases

Pain Assessment	Medical Procedures	Surgical Procedures
assessment	procedure	operation
evaluation	procedural pain	post-operative
intensity	medical procedure	postoperative
measure	Name of procedure, associated procedure or abbreviation e.g. cannulation, venepuncture, heelprick, heel prick, heel-lance, lance, needle, needlestick, vein, venous etc.	Name of procedure, associated procedure or abbreviation e.g. Adenoid, adenoidectomy, tonsil, tonsillar, tonsillectomy, adeno-tonsillectomy, adenotonsillectomy etc.
metric		
rating		
reliability		
scale		
score		
tool		
validity or validation		
Name of specific tool or abbreviation e.g. 'FLACC' etc		

Table 3: Inclusion and Exclusion criteria

Study inclusion criteria	**Study exclusion criteria**
English	Not in English
Studies in children	Studies in adults
Population clearly defined	Population unclear, mixed adults and children without subgroup reporting
Validating specified pain assessment tool/s	tools measuring stress, anxiety, sedation or other non-pain modality
Randomised control trials, meta-analyses or systematic reviews of RCTs, Cohort studies or Case series reporting efficacy data	Efficacy data incompletely or insufficiently reported
Procedure clearly defined	Procedure unclear or mixed/ unspecified procedures without subgroup reporting
	Chronic pain

Fig. 1 Search Strategy Example: Pubmed

1. **PubMed**
   http://www.ncbi.nlm.nih.gov/entrez/query.fcgi

2. **Limits**
   i) "**English**"
   ii) "**Humans**"
   iii) "**All Child: 0 -18 years**"

3. General Searches obtained using criteria:
   i) **child or children or paediatric or pediatric**
   ii) **acute pain or postoperative pain or analgesia**
   iii) specific procedure or keyword eg. "**tonsillectomy or tonsil"**

4. Searches i) - iii) combined using search "**History"** function.

5. Citations assessed for inclusion.

6. Expand function ("find related articles") used for key articles to broaden search.

7. Abstracts obtained and reviewed.

8. Full text articles obtained except where otherwise specified in data extraction tables

2.0 Appraisal of studies

Efficacy studies or other studies reporting efficacy data were appraised and graded for quality using the grading system recommended by the Scottish Intercolleageate Guideline Network (SIGN), shown below:

GRADE 1

1++
High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+
Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 -
Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

GRADE 2

2++
High quality systematic reviews of case-control or cohort studies. High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
2+
Well conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2 -
Case control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal

GRADE 3

Non-analytic studies, e.g. case reports, case series

GRADE 4

Expert opinion

This process was assisted by the use of study quality checklists: available from SIGN at www.sign.ac.uk/methodology/index.html. And using the 'Oxford Bias Guide' for the evaluation of clinical trials available at: http://www.jr2.ox.ac.uk/bandolier/Extraforbando/Bias.pdf .

3.0 Formulation of recommendations

Recommendations were formulated and graded according to the following criteria:

Grade A

At least one meta analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or
A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

Grade B

A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 1++ or 1+

Grade C

A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 2++

Grade D

Evidence level 3 or 4; or
Extrapolated evidence from studies rated as 2+

This process was assisted by reference to published guidance from the National Institute for Clinical Excellence (NICE) on creating guideline recommendations available at: http://www.nice.org.uk/page.aspx?o=423027

4.0 Good practice points

Good practice points are recommendations for best practice based on the clinical experience of the guideline development group, but not necessarily supported by research evidence.

5.0 Data Extraction Tables

1. Pain Assessment (see attached file)
2. Medical Procedures (see attached file)
3. Postoperative Pain (see attached file)

Committee on Psychosocial Aspects of Child and Family Health, American Academy of
Pediatrics; Task Force on Pain in Infants, Children, and Adolescents, American Pain Society. The
assessment and management of acute pain in infants, children, and adolescents. *Pediatrics*
2001;108(3):793-7.

Appendix 2

Implementation, Cost-effectiveness and Audit

It is the responsibility of heathcare organisations, such as hospital trusts, and of individual practitioners to ensure that decisions about health care are based on the best available, current, valid and relevant evidence.

Pain management in children is frequently identified as an area of practice in need of improvement. In the UK, the National Service Framework for Children has set standards in a number of areas of clinical practice, including pain management, which advocate the local implementation of evidence-based protocols and guidelines in order to achieve the highest standards of care(2003).

This document aims to assist this process by presenting background information and systematically derived evidence statements pertaining to the accurate assessment and effective management of acute pain during diagnostic and therapeutic procedures and following surgery in children.

The Association of Paediatric Anaesthetists will be responsible for the publication and dissemination of the document. The process of raising awareness will be assisted by the participation of the other professional organisations who have contributed to its development, including promotion of the document to their members.

Implementation

The document is designed such that individual practitioners can assess their own knowledge and performance against the stated advice and recommendations in relevant areas of their own practice.

At an organisational level, mechanisms should be put in place to ensure that current protocols and levels of care being provided are reviewed against the recommendations in the guideline or, where no protocol exists, one is developed in line with local preferences and circumstances. An algorithm for guideline implementation is given in Fig.1. The majority of hospital facilities used by children in the UK are covered by ‘Pain Control teams’, such teams can provide support such as help with the identification of a suitable implementation lead, assessments of current practice and teaching and training where needed. Further advice on implementation strategies are available from NICE (National Institute of Clinical Excellence), SIGN (Scottish Intercollegiate Guideline Network) and EPOC (Cochrane Effective Practice and Organisation of Care).

Cost-effectiveness

There is little or no data available on the cost effectiveness of acute pain management in children. Untreated pain adds considerably to the unpleasantness and trauma of illness, injury and clinical procedures: It is also likely to delay recovery and lead to long term adverse consequences(NSF 2003). The majority of analgesics, and specialised equipment such as PCA infusion pumps, mentioned in this guideline are already readily available in most hospitals. Nevertheless, additional resources may be required for e.g. staff training on the use of pain assessment tools or implementation of new analgesic strategies.

Audit

Implementation of the guideline should be reviewed and monitored regularly; including compliance with recommendations, the effectiveness of analgesic strategies and incidences of adverse effects. This is best achieved through regular audit using review of hospital records or by direct data collection from patients, their families or healthcare workers.

Examples of audit outcomes include:

Pain assessment		
Recommendation:	*Audit criterion*	*Outcomes*
No individual measure can be broadly recommended for pain assessment across all children or all contexts: Grade B	% patients having developmentally appropriate postoperative pain assessment	target 100%
Children's pain should be assessed, documented, and appropriate action taken: Grade D	% patients having documented pain assessments at predefined intervals following surgery	target 100%
	% patients receiving appropriate analgesia within pre-specified time interval following documented moderate/severe pain assessment.	target 100% within 15 minutes

Procedural Pain		
Recommendation:	*Audit criterion*	*Notes*
Venepuncture is preferred to heel lance (in neonates) as it is less painful: Grade A	% infants having heel lance	Heel lance may be necessary for some situations but it may also be possible to reduce incidence by appropriate modification of practice or protocols and re-audit
Behavioural techniques of pain management should be used to reduce Lumbar Puncture pain: Grade A Topical LA and LA infiltration are effective in reducing LP pain: Grade B	% patients having either LA and behavioural management technique or both.	Target 100%

Postoperative Pain		
Recommendation:	*Audit criterion*	*Notes*
A combination of individually titrated intraoperative opioids and regularly administered perioperative mild analgesics is required (tonsillectomy pain); Grade A	% patients with moderate/severe pain in postoperative recovery room	Target <20%
	% patients *prescribed* regular (as opposed to PRN) NSAID and Paracetamol	Target 100%
	% patients *administered* regular NSAID and Paracetamol	Target 100% Analgesics may be omitted for pragmatic reasons e.g 'patient sleeping' modifications of protocols e.g. change of route of administration, use of longer acting preparation. May reduce number of omitted doses.
Epidural analgesia with LA is effective following major abdominal surgery. The addition of opioid or clonidine may further improve analgesia but side effects are also increased: Grade B	% patients experiencing PONV, itching, drowsiness, hypotension etc during epidural analgesia	Assess rates of side effects and modify practice in order to reduce incidences. Re-audit

Fig 1. Algorithm or guideline implementation:

Is guideline relevant to our practice?

If yes

1. Identify an ‘Implementation-lead’
2. Carry out a baseline assessment of current practice

Does current practice comply with recommendations?

e.g.
Is developmentally appropriate pain assessment in use?
Are effective analgesic strategies available and in use?

If no

1. Identify areas needing action
2. Identify barriers to change (e.g. staff training, availability of analgesics or equipment)
3. Assess cost

Develop an action plan

Disseminate and implement plan

Review and monitor effectiveness

REFERENCES

Getting the right start: National Service Framework for Children.

National Institute of Clinical Excellence available at:
www.nice.org.uk/usingguidance/implementationtools/implementation_tools.jsp

Scottish Intercollegiate Guideline Network available at:
www.sign.ac.uk/guidelines/fulltext/50/section9.html

University of York. NHS Centre for Reviews and Dissemination. Getting Evidence into Practice. Effective Health Care 1999; 5 available at:
www.york.ac.uk/inst/crd/ehc51.pdf

Appendix 3

Research Implications

There have been substantial improvements in the quantity and quality of studies investigating the measurement and treatment of acute pain in children during the period covered by this guideline1996-2006. Nevertheless, only 1/3 of recommendations were based on evidence derived from randomised controlled trials assessed as being of the highest quality. The problems of conducting trials in children are well recognised, and have been discussed elsewhere, as have strategies and initiatives for overcoming them. Variability in trial design, heterogeneity in patient groups, lack of standardisation of outcome measures, low numbers of patients recruited into trials were frequently encountered drawbacks in the studies evaluated for this guideline.

I) Pain Assessment
More data is needed regarding the clinical utility and validity of the more popular pain assessment tools; particularly as this may lead to a greater consensus in the choice of tools for specific indications. Recent meta-analyses have been undertaken to determine the best validated tools for research purposes but again, more data is required. Pain assessment for children with neurodisability and impaired communication is very under-researched, and many more studies are needed.

II) Procedures and postoperative pain

Effectiveness
In general, studies often combined information from groups of children having very dissimilar types of procedure in a single study, making interpretation difficult. Where this was not the case data was sparse for many procedures, and some procedures could not be included because there was no data available at all. This was particularly true of more major (and rarer) operative procedures such as craniotomy or thoracotomy, but also some relatively commonplace types of surgery such as pyloromyotomy were also little studied.

There were few well-controlled trials comparing the efficacy of a ‘standard’ analgesic technique with an alternative approach; increased numbers of such trials would be an invaluable aid to clinical decision-making. As a consequence, it was rarely possible to make comparative statements about analgesic management strategies for a given procedure. More formal adoption of a commonly accepted standard analgesic strategy for certain procedures (to which other techniques could be compared) would facilitate trial design. Similarly, where one or more techniques have been found to be effective or partially effective there are few controlled comparisons of combinations of techniques against such a standard.

Studies of psychological techniques such as distraction or guided imagery frequently do not describe clearly the specific content of the intervention which makes comparison between studies difficult. Standardisation of such techniques e.g. by using a specified protocol or manual would assist with both further study and with implementation of strategies.

Risk-benefit

Clinical decision making always includes an evaluation of the possible risks and benefits of a particular pain management strategy for an individual patient and setting. Although many studies report side-effects, the small size of the majority of paediatric studies precludes assessment of the frequency of rarely occurring adverse effects although they may be of clinical significance e.g. neurological deficits following complex local anaesthetic techniques. Improved reporting of such effects and larger multicentre studies are needed that evaluate these risks and benefits for individual procedures and patient groups.

Cost-effectiveness

The cost effectiveness of interventions for acute pain management has been little studied. Increasingly, organisations providing heathcare require this kind of information before implementation of new strategies can be supported. Clearly this is an area of research in need of substantial development.

Appendix 4.0

Data extraction tables

Pain Assessment

AUTHOR	STUDY DESIGN/ TYPE	NO. OF PATIENTS /PARTICS	PATIENT/PART. CHARACTERISTICS	PAIN TOOLS USED	RESULT & CONCLUSION	LIMITATIONS	PROBLEMS	LEVEL. CMMNTS
Vetter & Heiner (1996)	Prospective, comparative study	n=30 children n=3 HCPs	8-16 years, (surgical procedures including orthopaedic, plastic, urologic, and general surgery)	VAS (0-10) - smiling anchor as 0. 10cm slide-rule. Independent pain-related behaviour score (0-100)	Variable and minimal correlation between VAS & observational score.	Pain related behaviour tool not validated.	The pain behaviour score not validated; just clinical impression based on facial expression, activity level and breathing pattern	2-
Foster & Varni. (2002)	A descriptive, correlational design. Phase 1: initial testing; Phase 2: instrument testing	n=55 parent/child dyads (n=5, phase 1; n=50, phase 2)	8-12 yrs 50% boys/50% girls Range of backgrounds.	The Child TQPM and Parent TQPM	Good criterion-related validity and initial support for construct validity were demonstrated	Smiley face used as anchor for no pain	Needs larger more diverse population to be tested on.	2-
Falanga et al. (2006)	Prospective comparative study of two independent groups	n = 112 n=56 in control group (n=25 girls, n= 31 boys). n= 56 in algorhythm group (n=18 girls, n=38 38 boys)	5-17 yrs Children post surgery, trauma or other painful medical conditions	VAS	Use of a standardised algorhythm = better analgesic outcomes. Improvement in child well being without increased opioid dosages.	Not randomised. Potential for contaminatio n. Focus on mod not severe pain. Use of VAS limits findings to children aged ≥ 5yrs Delay between 2 phases of study.		2--
Goodenough et al. (1997)	Comparative design	n=50 n=27 boys, n=23 girls	4-6yrs Routine immunization injection at clinic	Faces Pain Scale Poker Chip Tool Visual Analogue Toy Verbal Rating	Clinical utility demonstrated for FPS. Observer ratings: poor-mod correlation with self-report scores.	Small sample		2-

Von Baeyer & Spagrud (2007)	Systematic review	n/a	n/a	Observational (behavioural) tools	20 observational pain scales identified for review. Specific scales recommended for specific situations. No scale recommended for chronic or recurrent pain. No single observational measure is broadly recommended for pain.			2++
Yeh (2005)	Development, design and validation of Asian version of existing tool	n=370 Study 1: n=53 Study 2, n= 220 Study 3, n=149	3-7 years. Study 2: day care centre. Study 3: children post general anaesthetic for outpatient clinic surgery	Oucher Pain Intensity Scale (OPIS)- Asian Version, VAS, Hester's Poker Chip Tool (HPCT),	Children preferred to use the picture Oucher scale. Statistically significant differences in scores were obtained during pain	Final decision about pictures made by 'experts', not by children who will use the scale. Did not assess effect of		2++

				Child Medical Fears Scale (CMFS), Faces, legs activity, cry and consolability Pain Scale (FLACC) Scare scale.	episode for each of pain scales. Convergent, discriminant and clinical validity was proven for male & female version of Asian Oucher.	completing all the tools on the Asian Oucher.		
Ballantyne et al 1999	Randomized, crossover design to validate tool	n=43	24-40 weeks GA < 28 days of life at data Level III outborn neonatal intensive care unit	PIPP	Construct validity: good Inter- & intra-rater reliability: excellent. Clinical utility: high			2+
Stevens et al. 1996	Prospective and retrospective design to develop and validate tool			PIPP	Beginning content & construct validity demonstrated.	Convenience sample		2+
Ambuel et al.	Scale development	n=37 n=28 infants, n=17 preschoolers, n= 2 primary school	0-204 months In ITU receiving IMV or CPAP (various	COMFORT scale VAS	Inter-rater agreement & internal consistency: high. Criterion	Sample not representative of school-aged children & adolescents	Assessing distress rather than pain	2-

		children, n=3 adolescents. n= 17 boys, n=20 girls	diagnoses)		validity: high (assessed against PICU nurses global ratings) Suggests COMFORT scale is valid measure of children's distress as perceived by experienced clinicians			
Breau et al. (2001)	Observational videotape	n=123 n=67 boys n= 56 girls	4-5yrs Preschoolers receiving routine vaccinations. Varying past 'medical' experiences	Child Facial Coding System (CFC) VAS (used by parents). Faces Pain Scale (used by children).	Facial actions (pain face * brave face) change according to pain. Parents', children's and technicians' ratings correlate.	Limited generalisability to children of other ages. May not apply to intense pain situations (only 33 children rated pain as 3 or greater).		2-
Caljouw et al. (2007)	Repeated measures design	n=57 n=12 (28-29w); n=11 (30-31w); n=12 (32-33w); n=12	28-37 weeks gestational age; ≤7 days old	Adapted COMFORT scale VAS	Items of scale: high internal consistency. Valid & reliable instrument. Clinical utility.	Potentially not generalisable to seriously ill premature infants.		2-

		(34-35w); n=10 (36-37w)						
Van Dijk et al (2000)	Observational study to test reliability & validity of tool	n=158 n=56, 0-4 weeks; n=47, 1-6 months; n=23, 7-12 months; n=32 1-3 yrs	0-3yrs Neonates and toddlers after major abdominal or thoracic surgery	COMFORT scale VAS for pain.	COMFORT: inter-rater reliability good apart from 'respiratory response'. HR & BP measurement: limited validity. COMFORT does assess postop pain in population.	Relatively small sample size; multiple testing. Sample skewed (more infants than 1-3 year olds).		2-
Grunau et al. (1998)	Real-time observation based study	n=40	32 weeks gestational age	Neonatal Facial Coding System (NFCS)	Inter-observer reliability: high. Construct validity (at bedside): demonstrated.	Bed side coding of behaviour does not permit blinding of raters to events		2-
Hartrick & Kovan (2002)	Prospective single blinded observational study.	n=51 Stage 1: n=20 (postop pain) Stage 2: n=23 (non painful events) Stage 3: n=12	1-5 yrs Children emerging from general anaesthesia following elective oto-laryngology, urology & non painful	Toddler Preschooler Postoperative Pain Scale (TPPPS), Faces, Legs, Activity, Crying, Consolability scale (FLACC)	TPPPS, FLACC & modified COMFORT scale (used purely as a behavioural tool) can be recommended for postop assessment.	The act of scoring each tool may affect the scoring of the other tools. Only small sample so reduces power of statistical tests.		2-

			radiology procedures	COMFORT Scale (modified).	TPPPS: significantly better performance in discriminating between painful /non painful situations.			
Jonsdottir & Kristjansdottir (2005)	Crossover design	n=24 n=12 girls, n=12 boys	24 -42 weeks gestational age at birth < 28 days of life at data collection	Premature Infant Pain Profile (PIPP) - Icelandic Translation	PIPP measure is sensitive to a painful event & differentiates between stress & pain in a clinical context across linguistic barriers	Convenience sample		2-
Lilley et al. (1997)	Observational videotape based study	n=75 n=15, 2-4 months, n=15, 4-6 months, n=15, 6-12 months, n=15, 12-18, n=15, 18 months	2-18 months Infants undergoing routine immunization injections	Infant Characteristics Questionnaire (ICQ), Neonatal Facial Coding System (NFCS), Baby FACS.	Consistencies in facial displays over age groups. Differences on both measures of facial activity. Least pain expressed by four month age group.	Video recorder may have affected the infants' responses Face of the child sometimes also obstructed. Sub sample sizes: too low to infer statistical power to tests.		2-

					Temperament not related to the degree of pain expressed.	Age groups do not contain equal intervals.		
McNair et al. (2004)	Prospective, repeated measures, correlational design	n=51 n=6 (28-31 weeks; 5 boys, 1 girl) n=10 (32-35 weeks, 5 boys, 5 girls) N=36 (>36 weeks, 25 boys, 10 girls)	28–42 weeks gestational age Post surgery	PIPP CRIES VAS	Correlation indicated across the 3 measures. Convergent validity showed correlation, especially in 1st 24hrs. PIPP & CRIES valid for 1st 72 hrs post surgery.	Convenience sample The 2 surgical categories used would not necessarily be easy to replicate.		2-
Mathew & Mathew (2003)	Review paper	n/a	n/a	n/a	Identifies risk of adverse long term effects on infants. Preventative, therapeutic strategies, objective assessment & caregiver sensitivity	Review only		3

					identified as integral to good management.			
Lyon & Dawson (2003)	Evaluative literature review	n/a	n/a	Oucher Children's Hospital of Eastern Ontario Pain Scale (CHEOPS)	12 papers (3 addressing subject indirectly). Disagreement as to whether CHEOPS correlates to Oucher score. No agreement as to whether the CHEOPS is more/less reliable in different age groups.		Further studies needed, using a larger sample, in a range of clinical situations.	4
Merkel (2002)	Discussion of tool	n/a	n/a	Finger Span Scale	Discussion of potential for using scale for young children Proposed it could be used alongside tools such as FLACC.	No research evidence, no empirical evidence although potential benefits identified.	Still based on children understanding difference between 'a little' and 'a lot'	4

Breau et al (2002)	Longitudinal observational validation study	n=24 parents	3–19 yr Children with severe intellectual disabilities	Non-communicating Children's Pain Checklist–Postoperative Version (NCCPC-PV) VAS	Internally reliable. Interrater reliability: good. Sensitivity and specificity for classifying children with mod-severe pain Good psychometric properties. Potential clinical utility	Small sample size. Cut-off scores for inferring presence of mod-severe pain should be seen as preliminary		2+
Breau et al (2003)	Survey based attitudes study	n=65 n=52 parents n=13 health care providers	3-18yrs Children with significant cognitive impairment (17 months adaptive age - Vineland Adaptive Behavior Scale)	Pain Opinion Questionnaire	Caregivers believed children's pain sensation becomes greater relative to children without CI as severity of CI increases. Believed children with mild CI may over-react to pain. These beliefs	Caregivers' beliefs and experiences with their own child's pain may have influenced their responses. Expressed attitudes may not reflect expressed behaviour		2+

					could impact children's care.			
Breau et al (2000)		n= 55 n= 32 caregivers; part 1 of study n=33 caregivers	3-44 yrs individuals with cognitive impairments	Non-Commun-icating Children's Pain Checklist	Internal consistency exhibited. Sensitivity: good. Reliable over time. Good psychometric properties. Potential clinical utility.	Potential that endorsement of items could have been influenced by recall biases, or by a priori judgement that pain was occurring.		2+
Breau et al. (2001)	Determination of whether typical pain behaviour can predict future pain behaviour	n= 99 caregivers n=36 (sample 1); n=63 (sample 2)	Mean age 14yrs (sample 1) & 11yrs (sample 2) Individuals with cognitive impairments and with no ability to communicate verbally	Non-Commun-icating Children's Pain Checklist	Subset of items from NCCPC can predict pain	Heterogeneity of the groups in terms of diagnosis. CIs of the odds ratios generated for individual items were large		2+
Hunt et al. (2004)	Clinical validation study	n=140 n=76 girls, n= 64 boys	1-18yrs (mean age 9yrs, 11mnths)	Paediatric Pain Profile (PPP)	Internal consistency excellent. Face, concurrent &	Validity of proxy ratings open to question, although		2+

			Severe neurological & cognitive impairments		construct validity established. Reliable, valid tool. Potential clinical utility.	limited options within this population. Scorers not blinded to administration of analgesia		
Malviya et al. (2006)	Evaluation of validity & reliability of revised & individualised tool	n=52 12 children able to self-report using simple scale	4-19yrs Children with cognitive impairment	FLACC Simplified Faces Scale Verbal (0-10) Numbers Scale Simple Word Scale – (little, medium, big)	Interrater reliability: excellent. Criterion validity and construct validity demonstrated. Reliability & validity of FLACC for children with CI	Results limited to post-operative pain		2-
Voepel-Lewis et al. (2005)	Observational study	n=52 4 -19 years	4 -19 years Children with CI & their parents/guardians	FLACC Simplified Faces Scale Verbal (0-10) Numbers Scale SimpleWord	1 parent under-estimated, 3 parents over-estimated. Parents estimates of child's pain reasonable,	Results limited to postop. pain		2-

				Scale – (little, medium, big)	especially if using pain tool. Tendency to overestimate during the early postop period.			

Chambers et al. (1996)	Development & preliminary validation of tool	n=110 children (and parent) 56.4% male	7-12 years Day case surgery (high, moderate & low/no pain surgeries)	Parent's Postoperative Pain Measure Faces Pain Scale	Evidence of validity for 15-item PPPM for use with children (7-12yrs) following day surgery. Internally consistent and strongly related to child-rated pain.	External (inter-rater) reliability not assessed.		2-
Chambers et al. (2003)	Replication, extension of age group and validation study	n=158 children (& parent) n=51 children (7-12 yrs); n=22 girls, n=29 boys n=107 children (2-6 yrs); n=38 girls, n= 69 boys.	2-12 years Day surgery	Parent's Postoperative Pain Measure Faces Pain Scale (FPS)	Evidence of validity for 15-item PPPM demonstrated. Evidence of reliability & validity of PPPM as a measure of postoperative pain (2-12yrs)	External (inter-rater) reliability not assessed.		
Finley et a. (2003)	Development of construct validity of tool	n=103 Study 1: n=75; n=30 girls, n=45 boys	7-12 years Day surgery associated with at least moderate pain.	Parent's Postoperative Pain Measure Faces Pain Scale (FPS)	Evidence of validity for 15-item PPPM demonstrated.	External (inter-rater) reliability not assessed.		2-

		Study 2: n=28; n=7 girls, 21 boys		Stait-trait Anxiety Inventory for Children (STAIC).	PPPM can differentiate pain from anxiety. Further support for construct validity of the PPPM Confirmation as valid pain parental assessment tool for use at home following children's surgeries.			
Kankkunen et al. (2003)	Descriptive study of parents' perceptions	n=210 mothers n=114 fathers	Parents Children had undergone day surgery	VAS Parents Postoperative Pain Measure (PPPM) – Finnish version. Questionnaire	Parents' perceptions related to children's intensity & behaviours after surgery. Fathers accepted children's pain more than mothers. Boys expected to tolerate pain	Rating the pain intensity with VAS scores may have been difficult for some parents. Sample not representative of population	Doctors on strike during study period: impacted on questionnaire distribution; some surgeries cancelled.	2-

					more than girls			
Kokki et al. (2003)	Validation of existing tool in Finnish children	n=58 children (& parents)	1-6 yrs At home after minor day surgery	PPPM VAS Questionnaire	Construct validity was satisfactory. Convergence validity, predictive validity, internal consistency and equivalence all demonstrated.	Non random sampling & small sample size.		2-

de C Williams et al (2000)	Descriptive, qualitative-inductive interview design	n=78 n= 56 women n=22 men	Mean age 46 yrs (range 22±71 yrs)	VAS Numerical Rating Scales (NRS)	Lack of concordance between & consistency within patients suggests	Transferability to non chronic pain patients (and to child population)		2-

			Chronic pain patients		ratings incorporate multiple partially differentiated dimensions of pain. Lexical & numerical labels assigned to scale end-points affect use.			
Simons et al. (2001)	Phenomen-ological interview design	n=40 n=20 (parents) n=20 (nurses)	Children post-op from mod-major surgery		Parents felt their involvement was superficial & limited; their role was passive & expressed frustration.	Small sample. Children's perceptions not elicited.		2-
Simons & MacDonald (2006)	Action research (AR) – survey, audit & intervention	n=100 (survey)	Nurses	FLACC Wong & Baker Faces Tool VAS	Change (action) did occur but it was complex and barriers existed. Use of a pain assessment tool rose to	Time constraints limited engagement of participants. Some senior sisters did not engage/ support the		2-

					40% but some nurses still resistant.	AR.		
Simons & Roberson (2002)	Phenomen-ological matched interview, note review design	n=40 n= 20 (nurses) n=20 (parents)	Nurses & parents		Even when nurses' pain management knowledge was deficient, they expected parents to have a level of knowledge they did not possess. Poor commun-ication with parents evident & impeded effective pain management.	Small sample size. No respondent checking.		2-
Treadwell et al. (2002)	Quasi-experimental design – intervention, chart audit	n=85 children n=150 staff n=36 children; n= 68 staff (Time 1) n=49 children, n= 82 staff (Time 2)	Children primarily over 8 yrs of age; some 3-8yrs Staff: nurses, physicians, psychosocial staff.	Postoperative Pain Score CHEOPS Faces Scale NRS Word graphic scale APPT	Intervention enhanced pain assessment, staff responsive-ness, satisfaction with tools, compliance with pain assessment documentation	Convenience sample Lack of representation of children < 3 yrs. Caregiver & patient reports combined.		2-

Broome et al (1996)	Survey design	n=113 Healthcare professionals in teaching hospitals	Two-thirds nurses, one third doctors. Range of specialities.	Questionnaire	60% sample had standards of care/ protocols in place but only 25% followed these >80% time. Low likelihood of parental involvement prior to painful event	50% return rate. Inability to generalise outside of study population		3
Craig et al. (1996)	Literature review & proposal of a model	n/a	n/a	Conceptual model of children's pain proposed	Numerous deterrents to optimal care identified, common-place beliefs about the nature of pain in infants & children	Literature based.		3
Faries et al. (1991)	Comparative study	n=43 n=23 (control) n=20 (treatment group)	Adults Medical oncology	Pain Assessment Tool (PAT)	Treatment group reported significantly lower average pain intensity ratings than control.	Small scale. How transferable to child pain population & child nursing context.		3

Hodgins (2002)	Literature review	n/a	n/a	n/a	Utility of pain measurement is limited. HCPs no common understanding of meaning of scores generated by pain measurement tools. Instrument validity need to be broadened.			3
Karling et al. (2002)	Survey	n=299	Physicians and nurses		Under-treatment of children's pain primarily results from organisational issues & practices. Educational needs: high	Descriptive design		3
Polkki et al. (2002)	Survey	n=192 parents	8-12yrs Paediatric surgery wards	Survey	Non-pharma-cological methods: well utilized. Cognitive-behavioural & physical methods: less frequently	Questionnaires completed during child's hospitalization may have increased positive responses		3

					used. Child's gender, time of surgical procedure, & parents' assessments of child's pain intensity: significantly related to strategies used.	Dichotomous questions did not allow for indication of the frequency or intensity with which the non-pharmacological methods were used		
Salantera et al. (1999)	Non experimental survey study	n=267 nurses	Nurses working in children's departments	Survey	Overall, attitudes do not hinder effective pain management. Age, experience, place of work, field of expertise: no significant effect.	Convenience sample		3

Medical Procedures

INTERVENTION: Blood sampling, Venepuncture, and heel prick in neonates

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Jain and Rutter (2000)	RCT 27-41 weeks(med 33) 2 – 17 days n=40 (1 exclusion)	Amethocaine gel 1.5 g vs placebo for 1 hour prior to Venepuncture	Video recording of facial features and cry at 1 second intervals for 5 secs pre and post Venepuncture (neonatal facial coding system)	16/19 amethocaine treated infants showed little or no pain compared with 6/20 in the placebo group (p=0.001) Topical amethocaine provides effective pain relief during venepuncture in the newborn.	No local reaction seen	1 + (Tapes assessed by 2 observers)
Skogsdal et al (1997)	RCT Newborn N=120	1ml of 30% glucose vs breast milk and 10% glucose infants having heel prick. Not sucking		30% glucose alleviates mild pain		Grade 1+
Ogawa et al (2005)	RCT 5 days N=100	Heel lance alone Heel lance with pre treatment with oral sucrose Venepuncture alone Venepuncture with sucrose	Video recordings Neonatal facial coding system Crying response	Venepuncture is less painful and more effective than heel lance for blood sampling in newborn infants.($p<0.001$). Pre-treatment with sucrose significantly reduced	None	Grade 1+ Single blinded investigator

		Used 50% sucrose		(p<0.01)NCFS score for heel lance, but this remained significantly more painful during blood sampling than venepuncture alone(p<0.01) Sucrose pre-treatment tended still further to reduce the NCFS score for venepuncture, but this was not significant		

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Shah et al (2004)	Syst rev Term infants 4 trials included **(Cochrane**)	Venepuncture vs heel lance for blood sampling	Validated pain meaures	Venepuncture when performed by a skilled phlebotomist, appears to be the method of choice in term neonates	Needs more research in settings with multiple phlebotomists	1++
Logan (1999)	Controlled Clinical trial 36 newborns	Venepuncture vs heel lance for blood sampling	Audiotape of cry	Venepuncture: shorter sample collection time, length and duration of cry: p<0.05		2+ (Potential confounder is that midwives at 2 centres each did only 1 technique)
Taddio et al (1998)	Systematic review **Venepuncture** 2 studies: RCCT(n= 60)	**Venepuncture**: after application of EMLA or placebo Cohort design: EMLA vs no	Heart rate and cry Used Pain	EMLA associated with less pain as judged by HR and cry – no significance stated Pre-treatment with EMLA associated with a higher	Emla diminishes pain for circumcision but not heel prick. It may diminish	1+

	and nonrandomized (n=116) CCT Neonates **Heelprick** 2RCCT's: 67 infants	intervention **Heelprick** 0.5 g EMLA in 7 term infants vs placebo 0.5g EMLA in 60 preterm vs placebo	scores Crying during procedure PIPP profile	frequency of lower pain scores ($p<0.01$) No significant difference	pain for venepuncture, arterial puncture and percutaneous venous placement	

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Carbajal et al (2005)	RCCT Preterm: 27+/-1.7weeks N=42	Infants randomised to receive either morphine in a loading dose and then maintenance dose vs placebo: responses x 3 heel pricks before loading dose, 2 hours later and 24 hours later	Used Premature Infant Pain Profile	No significant difference in pain profile response to heel prick. Morphine does not provide adequate analgesia for acute procedural pain among preterm neonates		1+
Ling et al (2005)	RCCT Newborns admitted with jaundice N=52	Infants randomised to 2 ml oral 30% dextrose or 2 ml water pre venepuncture	Videotaped. Used Neonatal Infant Pain score and duration of cry	Dextrose group significantly less cry and pain as evinced by score (p0.03)		1+
Gradin et al (2005)	RCCT Newborns N=70	Heart rate monitored whilst infants given 30% glucose or water without painful stimulus	Observed heart rate	Significant increase in heart rate during glucose administration (p=0.002)	Important to recognise that effects of increase in heart rate during venepuncture may not be due to pain alone	1+

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Bauer et al (2004)	RCT Newborn(31 – 42 weeks) N=58	Randomised to 2 ml 30% glucose, 0.4 ml 30% glucose, or water.	Videotaped pain profile, , cry duration, indirect calorimetry and heart rate before venepuncture	2ml glucose reduced pain score compared with 0.4 ml and water but did not prevent rise on oxygen consumption, energy expenditure or heart rate	Suggests non painful handling causes stress – this may be reason for rise in 02 consumption despite 30% glucose	Grade 1+
Carbajal et al (2003)	RCT Newborn – term N=180	Gp 1: breast fed, gp 2: held in mothers arms , gp3 – given water, gp 4: 1ml 30%glucose followed by pacifier prior to venepuncture	Aigue Nouveau-ne scale and PIPP	Breast feeding and 30% glucose group both significantly better than other groups($p<0.0001$). No difference between these 2 groups	Breast feeding equivalent to 30% glucose + pacifier in terms of analgesia	Grade 1 +
Gradin et al (2002)	RCT Newborns N=201	Compared EMLA on skin +oral placebo, with Placebo on the skin and 30% glucose orally for venepuncture	Premature Infant Pain profile, heart rate and crying time	Pain scores and duration of crying were significantly lower in the glucose group than the EMLA group	Did not control for pacifier	Grade 1-

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Gradin et al (2004)	RCT Full term newborns N=120	During venepuncture: Gp 1 : breast fed and 1ml placebo, gp2 breast fed and 1 ml 30% glucose, gp3: fasting and placebo, gp4: fasting and 1ml 30% glucose	Premature infant Pain profile Crying time Parents rating on a Visual Analogue score	PIPP score significantly lower in infants receiving glucose(p-0.004) Breast feeding before venepuncture had no major impact on the pain score but reduced the crying time		1+
Carbajal et al (2002)	RCT – crossover trial Preterm neonates(< 32 weeks) N=40 (25 in trial1, 15 in trial2)	During sc injections of erythropoietin Trial 1: 0.3ml 30%glucose vs placebo Trial 2 0.3 mo 30% glucose with or without a pacifier	Pain using the Douleur Aigue Nouveau ne score	Significantly less pain with glucose vs placebo No additional effect of using a pacifier NB: 7 neonates in glucose group had slight but brief O2 desaturation.	These are very pre term infants – this could account for differences with sucking Recommend continous monitoring of preterm neonates receiving intervention	1+
Bellieni et al (2002)	RCT Newborn N=120	During heel prick: Gp A: Control Gp B:1ml 33% oral glucose+ sucking 2 mins before procedure Gp C: Sucking Gp D:1ml glucose +sucking GpE: Multisensory massage including 1 ml glucose+ sucking GpF: Multisensory massage	Video Assessment of pain using Douleur Aigue Nouveau ne score	Gp D and Gp E the most effective E> effective than D	(Pacifiers not used but syringe giving fluid used to stimulate sucking)	1+

		and placebo (mulit sensory massage massaging infant, talking to infant, allowing infant to smell perfume on therapists hands)				

INTERVENTION: Heelprick venepuncture PICC line insertion in infants

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Stevens et al (2004)	Sys Rev (Cochrane) RCT's in term and preterm infants – up to 28 days post 40 weeks gestational age Sucrose for analgesia in newborn infants	44 studies identified for inclusion in review 21 actually included (1616 infants) 9 evaluated preterm infants 11 term 1 both		Sucrose is safe and effective for reducing procedural pain from single painful events (heel lance, venepuncture). There was inconsistency in the dose of sucrose that was effective (dose range of 0.012 g to 0.12 g), and therefore an optimal dose to be used in preterm and/or term infants could not be identified. The use of repeated administrations of sucrose in neonates needs to be investigated as does the use of sucrose in combination with other behavioural (e.g., facilitated tucking, kangaroo care) and pharmacologic (e.g., morphine, fentanyl) interventions. Use of sucrose in neonates who are of very low birth weight, unstable and/or ventilated also needs to be addressed.	Suggested sucrose had greater analgesic effect when given 2 mins before painful stimulus	1++
Johnston et	RCT Preterm infants	Sucrose (0.1ml of 24%) or water given up to 3 times, 2	Neurobehaviour al Assessment	**No significant differences between the groups on any**	Not examined post discharge.	1-

al (2000)	<31 weeks at birth N=107	minutes apart for every invasive procedure over a 7 day period	of the Preterm Infant at 32, 36, and 40 week Neurobiological Risk score(NBRS) at 2 weeks of age and at discharge	**outcomes** but in sucrose group only higher numbers of doses predicted lower scores on motor development and vigour. In placebo group only higher numbers of interventions led to higher NBRS scores	Could only examine those not discharged to other centres at term.Concerns that < 32 week infants might potentially be at neurodevelopmental risk from too many doses of sucrose	
Stevens et al (2005)	RCT Preterm infants N=66	Gp1: standard care : positioning and swaddling Gp2: sterile water +pacifier Gp 3:sucrose 24% + pacifier Prior to all painful procedures	Clinical outcome data and neurobiological risk at 28 days of NICU discharge	No group differences for adverse effects or clinical outcomes or neurobiological risk status. Sucrose+ pacifier was effective and safe	Need further exploration of consistent pain management on clinical, developmental and neurobiological outcomes	1+

Taddio et al (2006)	RCT.Double blind. 132 neonates (mean gestation 30.6 weeks)	Randomized to receive tetracaine, morphine or both for alleviating pain in ventilated neonates prior to central line insertion. Separate non randomised control group	Pain score during different phases of procedure – and observed effect of drugs on need for ventilatory supposrt and skin reactions	Morphine and Morphine + tetracaine groups lower pain scores than tetracaine alone.	Morphine infants needed more ventilatory support, 30% tetracaine patients had skin reactions	1+
Carbajal et	RCT 150 newborns	Compared: no treatment Placebo(2ml	DAN score (a behavioural pain	Pacifiers more effective than sweet solutions alone.		1+

al (1999)	having newborn screening(venepuncture)	water) 2ml glucose 30% 2 ml 30% sucrose pacifier 2 ml 30% sucrose + pacifier	score)	Sucrose+ pacifier showed trend to lower score than pacifier alone		
Lemyre et al (2006)	RCT 54 infants 27+/- 2 weeks gestation requiring PICC lines	Tetracaine 4 % gel (Ametop ®) compared with placebo	PIPP score during initial venepuncture and then during insertion phase	No difference between the 2 groups	Infants PIPP scores were in the 'moderate' range suggesting that infants felt discomfort	1+

Shah et al (2006)	Cochrane review Effectiveness of breast feeding or breast milk in reducing procedural pain in neonates	11 studies identified		If available, breast feeding or breast milk should be used to alleviate procedural pain in infants undergoing a single painful procedure, compared to placebo, positioning or no intervention.Glucose/sucrose had similar effectiveness as breast feeding for reducing pain.	The effectiveness of breast feeding for repeated painful procedures is not established and further research is needed.	1++
Shah et al (1998)	RCT Double blind 75 term neonates undergoing heel prick	Randomised to receive 20 mg/ kg paracetamol or placebo 60 – 90 minutes before heel prick for newborn screening	Infant facial and cry duration.	No difference between the two groups – paracetamol does not reduce the pain of heel lance		1+
Cignacco et al (2007)	Systematic literature review of non pharmacological interventions management of procedural pain in preterm and term neonates	13 RCCT and 2 meta analyses were studied including: Nutritive and non nutritive sucking (5 papers). Music (2), facilitated tucking (3), swaddling(3), positioning (3), olfactory stimulation/multifactorial stimulation(2), kangaroo care/maternal touch(2)		of There is evidence that the methods of 'non nutritive sucking', 'swaddling' and 'facilitated tucking' have a pain relieving effect in neonates	Conclusions: Some of the non-pharmacological interventions have an evident favourable effect on pulse rate, respiration and oxygen saturation, on the reduction of motor activity, and on the excitation states after invasive measures. However, unambiguous evidence of this	1++

					still remains to be presented. Further research should emphasise the use of validated pain assessment instruments for the valuation of the pain-alleviating effect of non-pharmacological interventions.	
Barker et al (1994)	187 heel prick procedures in 47 infants	Randomly assigned 2 different lancet types - Autolet2 or Tenderfoot Preemie	Behavioural responses. Collection times.	No significant difference in behavioural response or times for collection of small to medium amounts of blood, but Tenderfoot device superior for large volumes(>1ml)	expensive	1-
Paes et al (1993)	40 health full term infants for newborn screening test	Randomized trial comparing automated lancet for heel pricks with manual device	Total blood, blood sampling times,pain (measured by crying times) and degree of bruising	Total volume and blood sampling time significantly better with automated lancet ($p<0.001$)	No difference in crying time	1-
Shepherd et al (2006)	340 healthy newborns undergoing screening test	Randomly assigned to heel prick via Tenderfoot or Genie-Lancet	Quality of sample Time taken No of heel pricks If needed to squeeze heel Pain expressed by infant	Tenderfoot device saved significant time, fewer no of heel pricks needed .	Pain assessed by length of cry only	1+

Shah et al (2003)	80 neonates – healthy undergoing newborn screening test	Compared BD safety flow lancet with BF QuikHeel	bruising Facial grimacing score during puncture and heel squeeze Cry duration, duration of the procedure, number of punctures required	QH group required fewer punctures and less crying. Pain scores during squeezing did not differ		1-

INTERVENTION: Examination for retinopathy of prematurity (ROP).

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Mitchell et al (2004)	RCT 30 preterm infants having ROP exams	Randomized to either: local anaesthetic eye drops+ pacifier+ 3 doses of sterile water or : local anaesthetic eye drops+ pacifier+ 3 doses of 24% sucrose during eye exam	Premature Infant Pain Profile (PIPP) measures physiological variables and behavioural state	During exam less distress in sucrose group but no difference after exam	Sucrose and a pacifier may be helpful during eye exam in infants who have already had local anaesthetic eye drops	1+
Grabska et al (2005)	32 infants RCT	Randomized to receive either sucrose or sterile water during eye exam	PIPP. Crying time	No significant difference between groups Sucrose group had small but significant drop in O2 sats after admin	Sucrose alone not sufficient Potential bias: infants described as being offered a pacifier but those receiving this intervention not separately considered	1-
Marsh et al (2005)	RCT 22 infants, < or = 30 weeks gestation	Randomized to either saline or proparacaine 0.5 % eye drops, receiving alternate treatment at second scheduled eye exam	PIPP – at 1 and 5 minutes before and after the eye exam and at insertion of the speculum	Significantly less pain at speculum insertion than with saline	Local anaesthetic drops should become routine practice	1+

Gal et al (2005)	RCT 23 infants < or = to 30 weeks	All had local anaesthetic drops. Randomized to receive either 2 ml of sucrose or 2 ml or water orally immediately prior to eye exam.	PIPP – at 1 and 5 minutes before and after the eye exam and at insertion of the speculum	For 3 of 5 responses significantly less pain at speculum insertion with sucrose than with placebo	Oral sucrose may reduce immediate pain response to eye exam	1+
Boyle et al (2006)	RCT 40 infants < 32 weeks gestation or birth weight blinded to study drug but not to pacifier	2 mins before first screening exam: either (i) 1 ml sterile water- syringe (ii) 1 ml sucrose 33% - syringe (iii) 1 ml sterile water – syringe +pacifier (iv) 1ml sucrose syringe+pacifier	Videotaped during exam and until 2 mins after. PIPP for 1st eye, physiological variables thereafter	Infants randomised to pacifiers scored significantly less than those without. Sucrose did not appear to have a synergistic effect in this study	Possible that a synergistic effect might be seen if repeated doses of sucrose given (see Mitchell)	1+

INTERVENTION: Lumbar puncture neonates and infants

.

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Crock et al (2003)	Questionnaire survey of children (< 18 years)with cancer and families undergoing repeated painful procedures eg LP or bone marrow (96 children)	Either midazolam sedation and local anaesthetic or GA	Questionnaire to children and parents about the procedure and which they preferred	GA: 106 procedures: restraint needed 4%. 25% reported distressed Sedation and LA: 94% procedures restraint needed, 90% reported distress	90% parents wished for GA for future procedures	Not further discussed in these tables but included to emphasise that children requiring repeated painful procedures should be offered GA option 3
Kanagasundaram et al (2001)	Observational study	Observational study of children receiving nitrous oxide in relieving pain and anxiety during painful procedures. 90 children requiring bone marrows, LP's, venous cannulation, dressing change	Observational Scale of behavioural distress scores pre, during and post procedure	Scores highest (most distress) during induction phase, with subsequesnt lower scores Most suitable for children over 6 and for short procedures	Few side effects . mean recovery time 3 minutes	2+
Kaur et al (2003)	Sixty consecutive newborns (gestational age, ≥34 weeks) undergoing diagnostic lumbar puncture	Topical application of 1 g of EMLA or placebo 60 to 90 minutes before lumbar puncture.	Heart rate, transcutaneous oxygen saturation level, and total behavioral score recorded on a video camera and graded	Lumbar puncture in newborns produces pain responses. Eutectic mixture of local anesthetics is an efficacious agent for reducing the pain associated with needle insertion and withdrawal during lumbar puncture in newborns.		1+

Carraccio et al (1996)	RCCT 100 infants less than 3 years requiring LP	Randomized to receiving lidocaine subcutaneously or placebo prior to LP	according to the Neonatal Facial Coding System. Comparison of number of attempts needed to obtain CSF and no of traumatic taps	No difference between groups in ease of obtaining CSF,. Slightly more traumatic taps in lidocaine group		1- Non blinded study
Uman et al (2006)	Cochrane review: Psychological interventions for needle related procedural pain and distress in children and adolescents	28 trials with 1951 participants age 2- 19 years. Only used RCT's with at least 5 participants in each arm comparing a psychological intervention group with a control or comparison group were eligible.		Largest effect sizes seen for treatment improvement over control exist for distraction, hypnosis, combined cognitive – behavioural interactions .	Health professionals should be aware of the value of incorporating psychological strategies for procedural pain and distress into practice with children	1++
Eidelman et al (2005)	Systematic review of randomised controlled trial 25 trials identified – 2096 subjects	Compared the analgesic efficacy of topical anaesthetics for dermal instrumentation with conventional local anaesthesia. Also compared other LA agents to EMLA		EMLA vs intradermal LA: no significant difference but EMLA advantageous because less painful to apply EMLA compared with tetracaine, liposome encapsulated tetracaine and liposome encapsulated lidocaine (ELA Max)	Liposomal lidocaine in the US is less expensive than EMLA and has a more rapid onset of action	**1++**
Stevens et al (2004)	Sys Rev (Cochrane) RCT's in term and preterm infants – up to	44 studies identified for inclusion in review 21 actually included		Sucrose is safe and effective for reducing procedural pain from single painful events (heel lance, venepuncture). There was	Suggested sucrose had greater analgesic effect when given 2 mins before	1++

	28 days post 40 weeks gestational age Sucrose for analgesia in newborn infants	(1616 infants) 9 evaluated preterm infants 11 term 1 both		inconsistency in the dose of sucrose that was effective (dose range of 0.012 g to 0.12 g), and therefore an optimal dose to be used in preterm and/or term infants could not be identified. The use of repeated administrations of sucrose in neonates needs to be investigated as does the use of sucrose in combination with other behavioural (e.g., facilitated tucking, kangaroo care) and pharmacologic (e.g., morphine, fentanyl) interventions. Use of sucrose in neonates who are of very low birth weight, unstable and/or ventilated also needs to be addressed.	painful stimulus	
Liossi et al (2006)	RCT Pediatric cancer patients requiring LP 45 children age 6 – 16 years	LP with 1. Local anaesthetic (LA) 2. LA + hypnosis 3. LA+ attention		LA + hypnosis group had less anticipatory anxiety and less procedure related pain and anxiety		1++

INTERVENTION: Chest Drain Insertion/ Removal

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Rosen et al (2000)	RCT n=120 children	0.1mg/Kg (10mg max) IV morphine v EMLA for CT removal EMLA on for 3hrs	pain assessed by observer using visual analogue scale 10cm	Before removal pain scores lower in morphine group. During procedure no difference between morphine (7.16) and EMLA (7.4) groups. Scores during procedure mod to severe pain.	no adverse events.	1+
Valenzuela (1999)	double blind RCT adults n=100	0.1mg/Kg (10mg max) IV morphine v EMLA for CT removal EMLA on for 3 hrs	Increase in pain from before to during CT removal Assessed by observer looking at pain behaviour VAS 10cm	No differences between the groups pre(morphine 0.4 EMLA 0.9) and post procedure Increase in pain during procedure less in EMLA (4.4 v 6.0 for morphine) group Conclude EMLA cream more effective than IV morphine in relieving pain of CT removal		1- 48 dropouts – no details. Implied that CT removed without observer present fewer patients able to complete questionnaire in morphine group

Bruce et al (2006a)	1 and 2 observational studies children study 3 pilot RCT children n=14	1. prevalence and clinical characteristics of pain and analgesic practices during CTR. N=135 2. efficacy and safety entonox for CTR. N=30 3. IV morphine versus entonox for CTR	Pain	1. prevalence mod to severe pain 76%. Morphine commonest used analgesic, varying dose. 2. Entonox safe still had pain despite also having morphine and/or diclofenac 3. no differences between morphine or entonox. Children still had pain. Morphine or entonox alone unlikely to provide adequate analgesia.		Studies 1 and 2 grade 3. Study 3 grade 1- (score 3), only pilot study. May not have been big enough to show difference
Akrofi et al (2005)	RCT Adults Post cardiac surgery N=66	0.1mg/KgIV morphine v 20ml 0.5% bupivicaine infiltrated subcutaneously v inhaled entonox for CTR	Pain measured on VAS 100mm	Pain scores: bupivicaine 9.5mm, entonox 37mm, morphine 15mm. Bupivicaine and morphine produce lower pain scores.	No differences in BP, heart rate, PaCO2, oxygenation or sedation	1- Pain scores low compared to other studies. All groups also had background morphine.
Puntillo et al (2004)	RCT Adults post cardiac surgery. N=74	4mg IV Morphine + procedural information v 30mg IV keterolac + procedural information v 4mg Iv morphine + procedural and sensory info v 30mg IV keterolac + procedural and sensory info. For CTR.	Pain intensity and distress before and straight after CTR.	No difference between groups. Pain level low in all groups. Either opiod or NSAID can successfully reduce pain during CTR if used correctly i.e big enough dose and given time to work.	No differences in sedation	1+ mean pain intensity score 3.26, Pain distress score 2.98. These are low.

Bruce et al (2006b)	Literature review 14 studies 5 descriptive 3 non-pharmological intervention 6 RCT (includes Rosen and Valenzuela) of morphine ,LA and entonox only 2 involved children.	Conclusions: Descriptive studies: 4 of adults. Suggest patients experience moderate to severe pain during chest drain removal. Type and dose analgesia given not reported. 1 of children didn't measure pain looked at behaviour, found displayed number of coping behaviours and concluded procedure frightening and painful. Non-pharmacological interventions: white noise, patients own music and no music – no difference. Relaxation technique v normal care – no difference. Ice v no ice – no difference. Patients given analgesia as well mainly opiates all experienced significant pain. Analgesic interventions: 3 morphine v LA, morphine v subfacial lidocaine – no difference. 2 morphine v EMLA (1 adult, 1 children) – EMLA group less pain. 1 LA (intrapleural bupivacaine via chest drain) v placebo - no difference both groups significant pain. Subgroup received IV keterolac – pain significantly lower in this group; 2 inhalation studies, entonox v entonox and 0.25% isoflurane – entonox only more pain, entonox v 0.25% isoflurane and 1% desflurane and 60% 02 – no difference. Pain mild but studies only briefly reported. Chest drain removal painful procedure. Non- pharmacological interventions not helpful. 4 of the 6 analgesic studies showed patients experienced mod to severe pain despite strong analgesics such as morphine and LA used. Morphine alone insufficient. Inhalation agents , NSAIDS and LAs may provide more effective analgesia. Multimodal therapy need more research.				3
Taddio et al (2006)	RCT.Double blind. 132 neonates (mean gestation 30.6 weeks)	Randomized to receive tetracaine, morphine or both for alleviating pain in ventilated neonates prior to central line insertion. Separate non randomised control group	Pain score during different phases of procedure – and observed effect of drugs on need for ventilatory supposrt and skin reactions	Morphine and Morphine + tetracaine groups lower pain scores than tetracaine alone.	Morphine infants needed more ventilatory support, 30% tetracaine patients had skin reactions	1+
Horsley et al (2006)	Cohort study of adults with small bore chest drains using historical controls			Seldinger drains were well tolerated and effective method of draining pneumothoraces and uncomplicated efdusion		3

INTERVENTION: NGT insertion

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Wolfe et al (2000)	double blind RCT adults n=40	atomized 4% lidocaine v saline to nasopharynx and oropharynx prior to NGT placement. all patients also received topical 2% lidocaine jelly intranasally.	Pain of NGT placement VAS 100mm	mean pain scores 37.4mm for lidocaine group and 64.5mm for placebo group. atomized 4% lidocaine results in clinically and statistically significant reductions in pain during NGT placement		1++ No children in this study
Singer et al (1999)	RCT Adults N=40	Topical anaesthetics and vasoconstrictors v surgical lubricants alone for NGT insertion. 0.5% phenylephrine spray to nose followed by 5ml 2% lidocaine gel. Throats sprayed with 2% tetracaine and 14% benzocaine	Pain NGT insertion measured on VAS Nasal pain, gagging, Vomiting , choking and epistaxis	Experimental group significantly less pain, discomfort and gagging. No difference in adverse effects	Use of topical lidocaine and phenylephrine to nose and tetracaine and benzocaine to throat significantly reduces pain and discomfort NGT insertion. Recommend widespread use.	1+ all adults ?children tolerate so much preparation
Ozucelik (2005)	RCT double blind Adults N=100	10mg metoclopramide IV versus saline IV as placebo for NGT insertion	Pain, nausea and discomfort VAS	Initaial VAS scores similar. Consequent scores sig lower in metoclopramide group.	Mean VAS scores for pain, nausea and discomfort significantly lower following IV metoclopramide	1++ Score 4 need IV access. no children

Cullen et al (2004)	RCT double blind Adults N=50	Nebulized lidocaine (4ml 10%) versus neb saline	Discomfort 100mm VAS	Lidocaine group mean VAS scores 37.7mm. Saline group mean VAS scores 59.3mm.	No difference in difficulty of procedure Epistaxis occurred more frequently in lidocaine group 17% v 0%. Neb lidocaine decreases discomfort of NGT insertion	1++ no children
Ducharme et al (2003)	Double blind double dummy randomized triple crossover Adults N=30	Healthy volunteers had 3 NGT placed acting as own controls for 3 medications: 1.5ml 4% atomized lidocaine, 1.5ml atomized cocaine, 5ml 2% lidocaine gel.	Pain of tube insertion and "global discomfort" Which do participants prefer?	No significant difference in pain scores. "global discomfort" less with lidocaine gel (p=0.17) Participants preferred gel	2% lidocaine gel appeared to provide best option.	1++ statistically but not clinically significant.
Stevens et al (2004)	Sys Rev (Cochrane) RCT's in term and preterm infants – up to 28 days post 40 weeks gestational age Sucrose for analgesia in	44 studies identified for inclusion in review 21 actually included (1616 infants) 9 evaluated preterm infants 11 term 1 both		Sucrose is safe and effective for reducing procedural pain from single painful events (heel lance, venepuncture). There was inconsistency in the dose of sucrose that was effective (dose range of 0.012 g to 0.12 g), and therefore an optimal dose to be used in	Suggested sucrose had greater analgesic effect when given 2 mins before painful stimulus	1++

	newborn infants			preterm and/or term infants could not be identified. The use of repeated administrations of sucrose in neonates needs to be investigated as does the use of sucrose in combination with other behavioural (e.g., facilitated tucking, kangaroo care) and pharmacologic (e.g., morphine, fentanyl) interventions. Use of sucrose in neonates who are of very low birth weight, unstable and/or ventilated also needs to be addressed.		

INTERVENTION: Venepuncture and intravenous cannulation in older children

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Eidelman te al (2005)	Systematic review of randomised controlled trial 25 trials identified – 2096 subjects	Compared the analgesic efficacy of topical anaesthetics for dermal instrumentation with conventional local anaesthesia. Also compared other LA agents to EMLA		EMLA vs intradermal LA: no significant difference but EMLA advantageous because less painful to apply EMLA compared with tetracaine, liposome encapsulated tetracaine and liposome encapsulated lidocaine (ELA Max)	Liposomal lidocaine in the US is less expensive than EMLA and has a more rapid onset of action	1++
Koh et al (2004)	RCT 8-17 years n=60	Comparison of 2 different topical anaesthetics: EMLA vs new ELA-Max	Children rated pain using visual analog scale. Anaesthetist rated presence of blanching and difficulty in siting iv	30 min application of ELA-Max as effective as 60 min application of EMLA. No difference in ease of venous access but less blanching with ELA-Max	ELA Max contains no prilocaine so that the theoretical problems of methaemoglobinaemia (not in practice a problem) – not a problem	1+
Luhmann et al (2004)	RCT 4-17 years n=69	Comparison of ELA-Max with 0.1-0.2ml sub cut buffered lidocaine in peripheral intravenous catheter placement	Self reported visual analog scale questionnaires for patients and parents, nurse and blinded observer	No difference between buffered lidocaine and ELA-Max in termsof pain, anxiety, technical difficulty		1+

Hee et al (2003)	RCT 8-15 years n=120	Day surgery patients needing iv's: Gp1:EMLA+air/O2 GP2:50%N2O/50%O2 Gp3:Emla +N2O	Childrens Hospital of E Ontario pain scale by observer, VAS by patien. Heart rate, O2 sats, ease of cannulation	EMLA and 50% nitrous oxide equally effective for pain reduction whilst combination provides superior analgesia and satisfaction	No difference in time or ease of cannulation	1-
Andrew et al (2002)	RCT 5-15 years n=80	Day surgery patients EMLA cream on each hand After removal and 10 mins prior to cannula, application of Glyceryl Trinitrate (GTN) ointment or placebo (each child their own control)	Hand with visually best quality vein selected and cannulated – primary outcome was which hand was selected	GTN hand was chosen in 70% of children suggesting that GTN cream may aid in cannula placement		1-
Taddio et al (2005)	RCT 1 month – 17 years n=142	Liposomal lidocaine or placebo prior to cannulation	Children<5 years pain evaluated by parents and research assistant(Face Pain Scale0 Over 5 years included child	Liposomal lidocaine associates with higher intravenous cannulation success rate	less pain , shorter procedure time and minor dermal changes with liposomal lidocaine	1+

Ekbom et al (2005)	RCT 6-18 years n=70 (50 with difficult venous access) 20 who very anxious	All had EMLA Randomized to N2O (NO) or conventional treatment	No of attempts at cannulation Time required for procedure Pain (VAS) Satisfaction score – parents, children and nurse	Highly significant results in both anxious children and difficult access children being easier and less painful in N2O group	Children held their own mask. Only suitable therefore over 6. Only tested very fit children (American Soc of Anaes – grade1). No problems – suggested gr 2 would also do well	1-
Kleiber et al (2001)	RCT Pre school children 44	Iv catheters placed for tests Parents received distraction education vs standard care	Observation of child and parent	No group differences in reports of behavioural distress. Parents who had been taught distraction were more likely to use it		1-
MacLaren et al (2005)	RCT 1-7 years n=88	Gp1: interactive toy distraction Gp2: passive movie distraction Gp3 : standard care	Parent, nurse, child over 4 self report; observational coding	Children in the passive condition were more distracted and less distressed than those either with interactive toy distraction of standard care – there were no differences between these groups (this was watching a movie rather than playing with an interactive toy)	Suggests a passive strategy is more effective method of distracting children than an active one – suggests children's distress interfered with their ability to engage with the distractor	1-
Uman et al (2006)	Cochrane review: Psychological interventions for needle related	28 trials with 1951 participants age 2- 19 years. Only used RCT's with at least 5 participants in each arm comparing a		Largest effect sizes seen for treatment improvement over control exist for distraction, hypnosis, combined cognitive – behavioural interactions .	Health professionals should be aware of the value of incorporating	1++

	procedural pain and distress in children and adolescents	psychological intervention group with a control or comparison group were eligible.			psychological strategies for procedural pain and distress into practice with children	

Fanurik et al (2000)	RCT 2-26 years in age blocks 2-4,5-8,9-12,13-16 n=160	Iv insertion in OP pre endoscopy All had EMLA Randomised to 'distraction' or 'usual coping strategy'	Pain ratings Behavioural distress ratings	Pain ratings not influenced by distraction but children's behavioural distress lower for older children and those who were provided distraction		1-
Kolk et al (2000)	RCT 3-8 years n=31	Children with local anaesthetic were randomly assigned to a have preparation before the Venepuncture or not	Groniger Distress Scale	Prepared children showed significantly less distress than those who had not been prepared		1- (small study)
McErlean et al (2003).	RCT 9months to 6 years n=46	Midazolam syrup pre placement of PIC	Parents and observers rated childrens pain scores	Median parents pain scores less in miazolam rather than placebo group (p=0.002) Observers scores not significantly different	No adverse effects in this small study	1-
Kanagasundaram et al (2001)	Cohort study Observational 90 children requiring repeated painful procedures	Gave between 50 and 70% NO to children between 1 and 11 years. Used OBSD-R scores during timed phases pre, during and post procedure	OBSD-R score	Increased level of distress during admin of NO – but this is less in children more than 6 years suggesting that those who can understand the procedure will benefit most	Children having dressing changes had higher scores than those having shorter procedures	2-

Costello et al (2006)	RCT 127 children between 9 and 18 years requiring intravenous cannulation	37 had ethyl vinyl chloride vapocoolant spray 48 received isopropyl alcohol (placebo) spray 42 no pre-treatment	Used children's VAS score	No difference between groups		1+
Davies and Molloy (2006)	RCT 77 children requiring venepuncture for assessment of GFR. Age 5 – 13 years	Compared ethyl chloride spray pre venepuncture with ametop	Childs preferred choice for third venepuncture having had one of each. Pain not assessed.	Equal preference		1-

INTERVENTION: Immunisation and IM injection

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Scheifele et al (2005)	RCT 4 – 5.5 years n=288	Compared local reactions at 48 hours and daily parental pain reports after 2 different diptheria-tetanus- pertussis vaccine booster doses at 4 – 6 years. The standard (DtaP) vaccine was compared with a vaccine containing a lower diptheria and pertussis doses (Tdap)	Daily parental pain reports. Assessment of degree of redness and swelling by nurse observer at 48 hours. Serological response pre and 4 weeks post vaccine	Less redness and swelling in the Tdap group at 48 hours. (p=0.004)Children with large reactions more likely to have higher levels of pre immunization ab levels. BOOSTER RESPONSES TO Tdap were reduced with the smaller antigen doses but generally satisfactory .	(No IPV in Tda	1++
Wood et al (2004)	Multi centre survey 4-6 years olds 28 paediatricians enrolled 620 children	Compared children pain scores post either 'Priorix' MMR vaccine of 'RORVax' MMR vaccine in children receiving their 2nd routine MMR vaccine. Children used a standardised 'faces pain scale'	Parents and childrens reports over 4 days post vaccination	Priorix less painful that RORVax (p<0.001) This persisted over 4 days		1- if all else equal , choice of vaccine influences degree of pain
Ipp et al (2004)	RCT Age = 12 months N=49	Random allocation to receive 'Priorix' or MMR-II .	Pain responses recorded before and 15 secs after immunization by parent and paediatrician,. Also recorded whether cried	Paediatrician (p=0.001)and parents (p=0.007) both scored pain scores significantly less for Priorix than for MMRII		1++

			and length of cry			
Ipp et al (2006)	RCT Double blind 4-6 years 60 children	Participants received either Priorix® or M-M-RII®	Children self reported 'Oucher ' scale. Parents and paediatricians completed VAS scores	MMRII group had higher median pain scores, crying and paediatrician reported pain		1+
Diggle et al (2006)	RCT 696 infants 2,3,4 months of age	Random allocation to immunisation with 23/25 mm needle, or 25 gauge 16mm needle; or 25 gauge 25 mm	Parental records of local and general reactions 6 hours post and 3 following days. Antibody response	No difference in antibody response Long needles reduce vaccine reactogenicity without compromising immunogenicity		1+
Uman et al (2006)	Cochrane review: Psychological interventions for needle related procedural pain and distress in children and adolescents	28 trials with 1951 participants age 2- 19 years. Only used RCT's with at least 5 participants in each arm comparing a psychological intervention group with a control or comparison group were eligible.		Largest effect sizes seen for treatment improvement over control exist for distraction, hypnosis, combined cognitive – behavioural interactions .	Health professionals should be aware of the value of incorporating psychological strategies for procedural pain and distress into practice with children	1++

Albertsen et al (2005)	RCT 12 children with ALL 17 treatment courses evaluated	Children receiving asparaginase. 4 different combinations: 2 where asparaginase dissolved in lidocaine and 2 in water	Pain intensity (Pain Visual Analog Scale, VAS score) and drug pharmokinetics evaluated	Pain scores showed significantly less pain if asparaginase dissolved in lidocaine ($p<0.0001$)	Did not affect bioavailability or absorbtion rate of the enzyme	1+
Amir et al (1998)	RCT Children receiving 2 doses of im benzathine penicillin for secondary prophylaxis of rheumatic fever 1 month apart N=18	2 groups: 1: benzathine penicillin diluted with sterile water, followed 1 month later with penicillin diluted with lidocaine 2: same regime in reverse order	Serum penicillin concentrations after each injection	Pain score significantly lower after lidocaine(? significance level)	No difference in serum penicillin levels	1-
Reis et al (2003)	RCT Infants receiving their routine 2 month immunizations (4 injections) N= 116	Intervention group: received sucrose, oral tactile stimulation with a pacifier or bottle, and were held by their parents during immunization. Control group did not receive these interventions (standard practice)	Blinded assessment of audiotaped crying, heart rate , parent preference for further use of injection technique, nurse rated ease of vaccine administration	Combining sucrose, oral tactile stimulation and parental holding was associated with significantly reduced crying ($p=0.002$).Parent preference for the intervention :$p<0.001$ (NB this part of the study not blinded)	Nurse rated ease of vaccine administration equivalent for both groups	1-

Lewindon et al (1998)	RCT 2,4, 6 months 107 infants	Received either 2ml 75% sucrose or 2 ml water pre immunisation	Duration of infant crying Infant distress assessed by visual analogue scale (Oucher)	Sucrose reduced infant crying time Mean duration of first cry reduced from 42 – 29 seconds.		1 -
O'Brien et al (2004)	RCT 1 year old infants n=120	1g amethocaine or placebo 30 mins before vaccination	Pain assessed by Modified Behavioural Pain Scale	4 %amethocaine reduces pain of immunisation (p = 0.29). Amethocaine produced local(non serious) side effects	No difference in immunization success. Needed applying 30 mins pre immunisation	1++
Taddio et al (1994)	RCT 0-1 years n=96	2.5 gm EMLA or placebo applied 60 minutes pre immunisation	Modified Behavioural Pain Scale and duration of infants cry	Time to cry longer with EMLA: p=0.0004 Total crying time shorter with EMLA: p = 0.027	EMLA group had more local skin reactions P<0.0001	!+

Lewkowski et al (2003)	RCT 9-11 years during immunisation 7-12 years during venepuncture	Compared: sweetened chewing gum Unsweetened chewing gum Sweet taste control	Ratings of pain intensity (not specified)	Variable correlation. Peer response may have affected girls ratings		2-
Cohen et al (2002a)	Controlled trial 3-7 years n=61	Compared procedural coping and stress behaviour in group of children trained in these skills compared to group who had not	Observation of children's ability to cope with immunization pain	Children understood coping skills but did not use them.	Observation showed that parents behaviour tended to comfort child distress, whearas nurse behaviour encouraged child coping	2
Cohen (2002b)	RCT Infants receiving immunization N=90	Compared nurse directed distraction to standard care during immunization (not blinded)	Observational scale Parent and nurse ratings Heart rate	Infants engaged in distraction and distraction reduced behavioural distress (? Significance level) Difference between ratings and heart rate inconclusive	Infants exhibited elevated stress prior to and during injection but this seemed to be fleeting	1-

Sparks et al (2001)	RCT 4 – 6 years n=105	Children needing DPT immunization.Randomly assigned to receive: Touch Bubble blowing Standard care	Child medical fear scale prior to injection. Pain of injection using Oucher scale	Both forms of distraction significantly reduced pain perception. Fear not a significant covariate but distraction effective when fear was not constant		1+
Cohen et al (1999)	RCT 10 year olds(4th graders) n=39 having 3 immunizations over a 6 month period	Compared distraction, EMLA, , typical care during immunization	Child and Adult medical Procedures Interaction	All children low distress despite moderate anxiety or pain. Distraction more child coping, less child distress. No difference in participant rating and heart rate with all treatments		2
Jackson et al (2006)	RCT 372 children, age 4 years, having 4th DtaP vaccine	Compared pre and ongoing treatment with either acataminophen(paracetamol) or ibuprofen or placebo to see if the local reaction could be modified	Size of local reaction to vaccine	No change between groups		1+

Mark et al (1999)	RCT 10 year old n=252	Compared DT vaccine given subcutaneously or intramuscularly in upper arm	Observed redness, itching, swelling, pain over 2 week period. Serology to look for ab levels	IM injection significantly less redness , swelling or pain. No difference in antibody responses.	Girls had lower response to diphtheria toxoid than boys	1+
Sweet and McGraph (1999)	Observational study Infants at 6 or 18 months N=60	Video recorded immunizations to see how different patterns of maternal and staff behaviour influenced prediction of pain	Neonatal Facial Action Coding System Child Adult Medical procedure Interaction scale	'Reassurance' ('mother's distress promoting behavior') predicted increased infant pain behaviour, whilst 'distraction'('staff coping promoting behaviour' predicted decreased infant pain behaviour		3
Cohen Reis et al (1997)	RCT School age children: 4 – 6years N=62	Immunization in following groups: Gp!: EMLA+distraction Gp2:Vapocoolant spray + distraction Gp 3 distraction	Videotape: cry duration Pain Behaviours as measured by Observational scale of Behavioural distress	EMLA and spray both significantly and equally better than control Children preferred vapocoolant	Vapocoolant much cheaper than EMLA	1+

Lindh et al (2003)	RCT 3 months n=90	Children receiving immunization EMLA + glucose Or placebo	ECG Video – modified behavioural pain scales (MBPS) Latent of first cry total crying time	ECG – transient heart rate slowing followed by acceleration significantly more in placebo group Cry and MBPS scores significantly less in EMLA+glucose group		1+
Cassidy et al (2001)	RCT 4-6 years n=161	Routine immunization EMLA patch vs placebo	Childs self report on a Faces Pain scale Child Facial Coding system Children's Hospital of E Ontario pain scale Parent and Technician ratings	EMLA patch group had significantly less pain on all 4 measures compared with placebo (17% vs 43 % in placebo group)		1+
Cohen et al (2006)	RCT 136 infants 1-24 months	Routine immunization Parents received coaching in distraction (watching 'Sesame Street' or 'Teletubbies' video versus standard care	MAISD (Measure of Adult and Infant Soothing and Distress) Parents and nurse rating using VAS	MAISD: infants in distraction group significantly less distress than control ($p<0.05$) No difference in parent and nurse report		1-
Jackson et al (2006)	RCT Blind 372 children	Routine immunization with 5th Dtap vaccine – compared pre treatment with paracetamol, ibuprofen or placebo	Local reaction with area of redness or limb swelling 48 post vaccination	No difference between groups		

INTERVENTION: Laceration repair

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Farion et al (2003)	Systematic review. 8 papers. Adults and children.	Tissue adhesives v standard wound closure. Acute, linear, low tension wounds.	Cosmesis Pain Procedure time	No difference in cosmesis. TAs less pain and quicker.	TAs slight increased risk of dehiscence.	1++ Same author and data as Cochrane review 2001. CD003326.
Barnett et al (1998)	RCT Children> 4yrs N=163	Glue versus sutures for repair linear lacerations ,5cm, ,12hrs old not involving eyelids or mucous membranes	Cosmetic outcome at 3 and 12 months	Cosmetic outcome the same.	Length time – glue group faster. Pain – doctors, nurses and parents but not children rated glue as less distressing	1-
Zempsky et al (2004)	RCT Ages 1-18 N=100	Steristrip versus dermabond for facial lacerations	Cosmesis at 2 months Pain.	No difference in cosmesis or pain scores	More dehiscence in dermabond group Equivalent techniques. Steri strips cheaper	1+
Hock et al (2002)	RCT Children 1-18 N=189	HAT v sutures	Procedure time Wound healing Scarring Pain Complications	HAT quicker, less scarring, pain and complications, trend towards better healing	HAT equally acceptable and perhaps superior to standard suturing	1+ score 3 not blinded

Eidelman et al (2004)	Systematic review. 22 trials	Topical v infiltrated anesthesia	Efficacy Cost ?need for cocaine	Topical as good or better analgesia than infiltrated anesthesia. Cocaine containing products costly and use not justified as equivalent efficacy		1++ scored studies using same scoring system as APA.
Ernst et al (1997)	RCT N=66 Only 13 were children (5-17yrs)	LAT v injected buffered lidocaine	Pain application or injection Analgesic efficacy	LAT less painful than injection. Equal efficacy. Trend towards LAT working better on scalp and face lacerations cf extremities	LAT gel compares favourably with injected lidocaine interms of anesthesia and considerably less painful to apply.	1+
White et al (2004)	Prospective case series. N=67 Ages 5-18	Lat for repair simple finger lacerations	LAT success/failure	53.7% success rate. Better anesthesia on dorsal than ventral surface.	No digital ischaemia. Safe and effective	3
Smith et al (1998)	RCT N=90 >1 year	Tetralidophen v lidocaine infiltration in repair mucous membranes.	Pain	Suture technician, research assistant and video reviewer scored lidocaine infiltration better. Patients and parents no significant difference in scores	Infiltrated lidocaine better but differences in pain scores were small and may not be clinically significant. Also pain of injection not taken into account	1-

Singer et al (2001)	RCT double blind Age 1-59 years N=60	Pretreat lacerations with either LET or Emla	Adequacy of anesthesia to needlestick. Pain of infiltration of lidocaine.	LET better at anesthesia to needlestick. No difference between the two in decreasing pain of infiltration.	Pretreatment with LET or EMLA results in similar amounts of pain of subsequent lidocaine infiltration. LET cheaper and not contraindicated in open wounds.	1++ 2/3 patients <18yrs
Singer et al (2000)	Double blind RCT N=43 Ages >1 year mean age 13yrs	Pretreatment with LET V placebo	Adequacey of anaesthesia to needlestick. Pain of infiltration of lidocaine.	LET group better anaesthesia to needlestick and significantly less pain on infiltration of lidocaine	Pre-treatment with topical LET significantly reduces pain of subsequent lidocaine injection	1++
Stewart et al (1998)	Double blind RCT N=100 Ages 5-16 years	Aqueous 1% lidocaine or saline soaked pad applied to wound 10 min prior to infiltration of lidocaine.	Pain response from patient and parent	No difference	Topical lidocaine ineffective at relieving pain of injection.	1++
Luhmann et al (2001)	RCT Ages 2-6 years N=204	Standard care (topical +/- infiltrated anesthesia) v standard + N_2O v standard + oral midazolam v standard + N_2O and midazolam	Distress during procedure scored by observer (OSBD-R)	Groups that received N_2O had lower distress scores. Groups that received midazolam had more adverse events and longer recovery times.	Regimens including N_2O more effective at reducing distress during suturing of facial lacerations in 2-6 year olds	1+

Burton et al (1998)	Double blind RCT N=30 Ages 2-7 years	50% NO/ 50% oxygen versus 100% oxygen for laceration repair.	Change in Pain (CHEOPS) and anxiety scores before and during laceration repair	Pain and anxiety scores went up in control group and down in NO group.	NO/oxygen mix significant decrease in anxiety during laceration repair	1+
Davies et al (2003)	Systematic review. 63 publications. 22 RCTs	Buffering local anaesthetic with sodium bicarbonate	Pain of infiltration	Buffering significantly reduces pain of LA injection	Buffering significantly reduces pain of injection. Particularly useful for large or sensitive areas and in children.	1++
Bar-Meir et al (2006)	Observational study 60 patients between 1 and 16 years requiring suturing	15 received standard care and 45 had nitrous oxide in addition to lidocaine infiltration	Pain scores evaluated by surgeon and nurse at end of procedure using FLACC scale	FLACC scores lower in nitrous oxide group	.3% of children had mild side effects – mostly nausea and vomiting	2-
Sinha et al (2006)	240 children between 6 and 18 years requiring suturing	Age appropriate distractors or a control group	Facial Pain scale State trait anxiety inventory in over 10 year olds	Nodifference in facial pain scores in children less than 10 although parents perceived less distress. Older children had reduced situational anxiety but not pain intensity or parents perception of pain distress	Older children may benefit from distraction in terms of anxiety but need further pain management	1 -

Das et al (2005)	RCT 7 children acted as own controls. 11 episodes studied ages 5-18	Playing a vitual reality game + analgesia versus analgesia alone during burn dressing changes	Pain during removal and application of dressing. Parent and nurses view of child's anxiety and perception of pain.	VR significantly reduced pain during dressing change – by at least 2 on FACES scale. Parents and nurses agreed VR reduced anxiety and pain.	No side effects	1+ Small study Some children studied more than once.
Fratianne et al (2001)	RCT crossover N=25 Ages 7+	Music therapy versus no music therapy during dressing changes	Patients perception pain and anxiety. Nurses observation of patient's tension	Significant reduction in self-reporting of pain in those who received music therapy. Biggest difference at beginning and end of treatment. During debridement less effective.		1- not blinded. Need therapist present.
Hernadez-Reif et al (2001)	RCT n=24 age – mean 2.5 years	Massage therapy versus no massage therapy in addition to standard care during dressing changes.	Observers perception of distress behaviours (CHEOPS) Nurses perception of ease in completing procedure	Massage therapy group showed less distress (facial grimacing, torso movement, crying, leg movement and reaching out) Nurses reported easier to complete dressing		1+ Massage 15min prior to dressing change.
Robert et al (2003)	RCT double blind reverse crossover. N=8	Oral Morphine versus transmucosal fetanyl citrate during tubbing	Pain (FACES scale) and anxiety (FEAR Thermometer)	Pain and anxiety better managed with fetanyl		1- no details randomization or double blinding. Small study.

	Age 5 -/+ 2					
Borland et al (2005)	RCT double blind crossover N=24 Median age 4.5 years (max 15 years)	Oral morphine versus intranasal fetanyl	Pain scores	No significant difference in pain scores	Time to resumption normal activities. No significant difference. Fewer side effects with INF. INF suitable analgesic	1++ no details randomization.
Sharar et al (1998)	RCT double blind crossover N=14 Ages 4-17 years	Transmucosal fetanyl versusoral hydromorphone for wound care	Patient pain scores. Observer scores for co-operation, anxiety and sedation.	Fetanyl improved pain and anxiety scores during wound care.	No significant difference in vital signs, n&v, pulse oximetry, sedation , cooperation or time to normal activites. Fetanyl safe and effective. Minor improvements in analgesia and anxiolysis.	1+
Sharar et al (2002)	Double blind RCT placebo controlled	Oral transmucosal fetanyl citrate versus oral oxycodone for outpatient wound care	Patient pain scores. Observer scores	No significant differences	No significant side effects.OTFC and oral oxycodone	1+

	N= 22 Ages 5-14 years	procedures.	for cooperation, anxiety and sedation.		safe and effective in outpatient setting. Fetanyl improved palatability	no details randomization. Dropouts not discussed.
Heinrich et al (2004)	Case Series N=47 dressing changes (30 children)	PR S(+)-ketamine and midazolam for dressing changes in outpatient setting.	Pain Patient satisfaction	94% adequate sedation and analgesia Return to normal after 30 min All children had anterograde amnesia No complications	Conscious sedation with rectal S(+) ketamine and midazolam safe and effective	3 sedation

INTERVENTION: Bladder catherisation older children

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Rogers et al (2006)	RCT 80 infants less than 90 days.	Infants less than 90 days requiring bladder catheterisation in the Emergency department randomised to 24 % sucrose or placebo immediately before the procedure.	Pain scores, presence of cry, time to return to baseline	Overall, no effect of sucrose seen on pain scores between the two groups.	Subgroup analysis of the patients less than 30 days suggested that the sucrose group had less pain	1+
Phillips et al (1998)	35 children undergoing MCUG Cohort study	Parents given different ways of explaining MCUG to their child – either story booklet or story booklet and play.	Child's reaction to investigation assessed by using Gronigen Distress Rating Scale and parents coping style associated with Utrecht Coping list.	Parents giving truthful explanation reported considerably less distress than those whose parents had avoided upsetting details		2-
Vaughan et al (2005)	RCT Double blind 2 years or less 115 patients	2% lidocaine gel versus non anaethetic lubricant applied to both genital mucosa and catheter (not applied directly to penile urethra)	FLACC scale – pain measured before, during and after catheterisation	Both groups had increase in pain scores. Anesthetic gel did not show significant difference	? would it have made a difference if applied directly to penile urethra)	1-

Butler et al (2005)	RCT not blinded 46 children ll of whom had had a previous MCUG and had found this distressing	Children offered routine care (play visualization, breathing exercises) versus hypnosis. Children seen by researcher on day before procedure then had a 1 hour training session in imaginative self hypnosis which they then practised. Therapist also present when child undergoing MCUG	Child and parental reports of distress compared with previous one, observers ratings of distress, medical staff reports of the difficulty of the procedure and total procedural time	Significantly less distress in hypnosis group		1-
Kozer et al (2006)	58 infants less than 2 months old, and requiring a urine sample for investigation of fever	randomly assigned to an SPA (with EMLA) or bladder catheterisation with local anaesthetic gel	Investigator blinded to the procedure scored videotapes of infant behaviour using DAN score. Also nurse and parent ranked infants pain	SPA more painful than TUC	Parent and nurse observation, duration of cry and success rate in obtaining urine	1+

Uman et al (2006)	Cochrane review: Psychological interventions for needle related procedural pain and distress in children and adolescents	28 trials with 1951 participants age 2- 19 years. Only used RCT's with at least 5 participants in each arm comparing a psychological intervention group with a control or comparison group were eligible.		Largest effect sizes seen for treatment improvement over control exist for distraction,hypnosis, combined cognitive – behavioural interactions .	Health professionals should be aware of the value of incorporating psychological strategies for procedural pain and distress into practice with children	1++

Surgical Procedures

INTERVENTION: myringotomy

AUTHOR	DESIGN	TREATMENT	OUTCOME	RESULT	S-EFFECT / 2^0 OUT.	EVIDENCE LEVEL / COMMENT
Bean-Lijewski, (1997)	DB RCT 6/12-9yrs n=125	Paracetamol 15mg/kg Ketorolac 1mg/kg Oral 30 mins preop	Obj Pain Scale 5, 10, 20mins	K pain score lwr 5 and 10 min only (both below extra treatment trigger); No diff at D/c or post D/c analgesia	No diff	1+
Bennie (1997)	DB RCT >6/12 n=43 (13-16 each grp)	Paracetamol 15mg/kg Ibuprofen 10mg/kg Saline Oral 30 mins preop	CHEOPS 5,10,15,30,45, 60 mins after surgery	No diff in pain scores cf. placebo; no diff in rescue cf. placebo	No diff	1- Small sample
Bolton (2002)	Open label (mainly ph'kinetic study) 17-72 mths n=30	Paracetamol 40mg/kg oral 30 mins preop	CHEOPS 10,20,30 mins	57% no further analgesia		2-
Bennie (1998)	DB RCT >6/12 n=60 (15 each grp)	Transnasal butorphanol 5, 15, or 25mcg/kg saline	CHEOPS 5,10,15,30,45, 60 mins after surgery	25mcg: lwr pain score, incr time to analgesia; lwr doses no diff from placebo	No diff in vomiting; incr sedation and time to oral intake with 25mcg	1- small sample size
Galinkin (2000)	Randomised not blinded (mainly ph'kinetic) 9/12-6yrs n=265	Intranasal fentanyl 2mcg/kg; Saline; ALL: paracetamol 10mg/kg	CHEOPS 5 then 15 minutely until 2hrs	Decr CHEOPS	Incr time to discharge from recovery; no diff vomiting	2+ Minor decr pain score – not clin significant

Pappas (2003)	RCT single blinded 6/12-6yrs; n=120	Paracetamol 10mg/kg; Parac 10mg/kg + codeine 1mg/kg; Nasal butorphanol 25mcg/kg; IM ketorolac 1mg/kg	Obj pain score (0-10)	Higher pain score in P and P+C cf. B and K; incr rescue in P; no diff in analgesia at home	Incr vomiting in P+C and B	1- statistical not clinically significant difference in pain scores
Tobias (1995)	Rand ?blinded 6-60mths n=50	Paracetamol 15mg/kg; paracet 10mg/kg + codeine 1mg/kg; Oral 30mins preop	Observer pain scale (0-10) 5 and 30 mins	Decrease pain score P+C; decr suppt analgesia		2+ Statistical but minimal clinical significant decr score
Watcha (1992)	DB RCT n=90	Paracetamol 10mg/kg; Ketorolac 1mg/kg; Saline. Oral 30 mins preop	Obj pain scale	K: lwr pain score and less suppt analgesia; P no different from placebo		1-
Tay (2002)	DB RCT >1yr n=63	Paracetamol 15mg/kg; Diclofenac 0.5mg/kg [all fent 1mcg/kg]	CHEOPS	Pain scores low and no diff; 20-27% require rescue		1+ all received fentanyl
Ragg (1997)	DB RCT 1-12 yrs n=95	Paracetamol 20mg/kg; parac 12mg/kg + codeine 0.5mg/kg + promethazine 0.65mg/kg		Pain scores low and similar both grps	sedation and time to oral intake increase with combination	1+
Bhananker (2006)	DB RCT (comp gen.) 6mths-8yrs n=124 (52/72)	Paracetamol 30mg/kg preop + saline ear drops vs placebo + 2%lignocaine ear drops	CHEOPS (0-10) 5 minutely in PACU; Paracetamol 15mg/kg rescue score >6 - codeine if no response; parent VAS at home at home, going to bed, next morning	Pain scores no diff; %requiring supplt analgesia no diff		1+
Derkay (1998)	DB RCT (?method) Age: 4mths-	Paracetamol 10mg/kg; Paracet 10mg/kg + codeine 1mg/kg;	Obj Pain score 0-10 arrival, 15 & 30 mins	Pain scores no diff in PACU and 24hrs; Suppt analgesia 24hrs: no diff	No facial nerve palsy, 1/200 vertigo	2+

	18yrs n=200	Ibuprofen 10mg/kg; Placebo (all preop) ALL: 4% lignocaine				
Lawhorn (1996)	DB RCT Children N=122	4% lignocaine drops at end BSM		Decr pain score; decr % req. suppt paracetamol	No vertigo or tinnitus	1-

INTERVENTION: tonsillectomy meta-analyses

AUTHOR	DESIGN	TREATMENT	OUTCOME	RESULT	COMMENTS	Gr
Cardwell (2005)	Meta-analysis Cochrane	NSAID and tonsillectomy 13 trials, n=955 children	Bleeding requiring surgical intervention	NSAIDs did not significantly alter no. of periop bleeding events needing surgery OR no. of bleeding events not requiring surgery	Bleeding req. surgery rare – large CI (0.42-4.28) suggests need further studies Subgroup analysis ketorolac: no significant diff in bleeding	1++
Marret (2003)	Meta-analysis	NSAID and bleeding Adult and paed 7 studies. Adult and paed	Postop bleeding No. reoperation	Bleeding incr 5.3 to 9.2% OR 1.8(0.9-3.4) Reop incr 0.8 to 4.2%; OR 3.8(1.3-11.5) NNH 29	"NSAID should not be used" 114/262 receiving NSAID = ketorolac 1mg/kg	1++
Krishna (2001)	Meta-analysis	Aspirin vs NSAID (ibuprofen & diclofenac) 7 studies, Adult and paed	Postop bleeding	aspirin OR 1.94 (1.09-3.42) significantly higher than NSAID OR 0.93(0.44-1.95)	limited literature review – mainly ENT journals	1-
Moiniche (2003)	Quantitative systematic review	NSAID and tonsillectomy 25 studies, NSAID n=970, nonNSAID or placebo n=833. Adult and paed	Intraop blood loss Postop bleeding Hospital admission Reoperation for bleeding	Postoperative bleeding: ns Only reoperation happened significantly more often with NSAID OR: 1.12-4.83; NNH: 60(34-277)	"should be used cautiously…further research needed rather than clinical recommendations"	1++
Moiniche (2003)	Quantitative systematic review	NSAID vs opioid Adult and paed	PONV	Risk of emesis signif. decreased: 31.6% vs 48.8% RR 0.73 (0.63-0.85), NNT 9		1++
Cardwell (2005)	Meta-analysis Cochrane	NSAID and tonsillectomy 10 trials, n=837 children	PONV	Less nausea and vomiting when NSAID part of analgesic regime		1++

Steward (2003)	Meta-analysis Cochrane	Single intraop dose dexamethasone and post-tonsil morbidity; Paed	PONV	Single intraop dose (0.15-1mg/kg; max dose 8-25mg) 2 times less likely to vomit; NNT 4 More likely soft/solid diet on day 1 (RR 1.69; 1.02-2.79)	Missing data and variant measurement tools – unable to assess effect on pain	1++
Moiniche (2003)	Quantitative systematic review	NSAID vs placebo and vs opioid Adult and paed	Analgesia	NSAID vs placebo: 10/11 studies improved pain relief NSAID vs opioid: 8 studies: NSAID > opioid in 2; equianalgesic in 5; NSAID < opioid in 1 NSAID vs paracetamol: 3 studies : all no diff NSAID vs paracetamol & codeine: 3 studies: 1 each <,>,=	Opioids: morph 0.1-0.2mg/kg; papaveretum 0.2-0.3mg/kg; pethidine 1mg/kg; tilidine 2.5mg/kg; orqal tramadol 1mg/kg)	1++
Hollis (2000)	Meta-analysis Cochrane 6 trails	LA either injected before or after removal (5); spray after removal (1)	Pain score Supplemental analgesia	No significant difference	Small no. of trials and small sample sizes	1+
Hamunen (2005)*	Systematic review 36 studies 16/36 sensitive	Pain after tonsillectomy: paracetamol, NSAIDs, opioids. Age 1-16yrs	Analgesia	See summary and table below	Heterogeneity of data precluded meta-analysis	1++

Summary Table from Hamunen, 2005*

AUTHOR	STUDY ANALGESIC	ROUTINE ADDITIONAL ANALGESIC	MAIN RESULT
Bone (1988)	Diclofenac 2mg/kg PR vs. papaveretum 0.2mg/kg IM vs placebo	No	Decrease rescue analgesia with diclofenac
Ozkose (2000)	Tramadol 0.5mg/kg vs. tramadol 1mg/kg vs placebo	No	No difference in rescue analgesia or pain intensity
Sutters (1995)	Ketorolac 1mg/kg IM vs. placebo	No	Ketorolac reduced rescue analgesia and pain intensity

Watters (1988)	Pethidine 1mg/kg IM vs diclofenac 1mg/kg IM vs control	No	Pethidine and diclofenac equal need for and time to rescue, and pain intensity
Anderson (1996)	Paracetamol 40mg/kg oral preop vs 40mg/kg PR at induction	No	Oral: less rescue morphine in PACU and lower pain scores
Habre (1997)	Nalbuphine 0.1mg/kg IV vs. pethidine 1mg/kg IV	Paracetamol 15mg/kg po preop	Nalbuphine: higher pain scores and more rescue in PACU
Mather (1995)	Paracetamol 20mg/kg po preop vs morphine 0.1mg/kg IV vs. paracetamol 20mg/kg preop + ketorolac 0.5mg/kg IM during	No	Paracetamol alone: more morphine compared to other groups
Mendham (1996)	Diclofenac 1mg/kg PR vs. diclofenac 1mg/kg PR + fentanyl 0.75mcg/kg IV vs. tenoxicam 0.4mg/kg IV vs. tenoxicam 0.4mg/kg + fentanyl 0.75mcg/kg IV	Paracetamol 15mg/kg qid + diclofenac 1mg/kg tds	Tenoxicam alone: higher pain score in PACU and more rescue cf. diclofenac alone
Moore (1988)	Fentanyl 1mcg/kg vs. nil	Pethidine 1mg/kg IM preop	Fentanyl: pain score lower at 10 and 20 mins; less rescue analgesia
Oztekin (2002)	Diclofenac 1mg/kg PR vs nil	Remifentnil infusion, morphine 50mcg/kg at end + PCA postop (bolus+4mcg/kg background)	Diclofenac: lower pain score first hour, lower total morphine consumption
Pendeville (2000)	Tramadol 3mg/kg IV +2.5mg/kg po at 6hrs postop then tds vs. Propacetamol 30mg/kg IV + 15mg/kg 6hrs postop then tds	Sufentanil 0.25mcg/kg IV	Tramadol: lower pain scores (PACU, ward & home); less rescue
Pickering (2002)	Ibuprofen 5mg/kg po vs. rofecoxib 0.625mg/kg po vs. placebo (1/24 preop)	Paracetamol 20mg/kg po 1/24 preop + fentanyl 2mcg/kg IV	Ibuprofen: less early rescue. No diff in time to first rescue, pain score at 4/24, total analgesic consumption
Romsing (1998)	Ketorolac 1mg/kg at induction vs. after surgery vs. placebo	Fentanyl 3mcg/kg IV, paracetamol 20mg/kg	Preop ketorolac less rescue in PACU vs postop ketorolac. No difference in rescue during first 5/24 in ketorolac grps. No difference in paracetamol during 24/24
Sutherland (1998)	Tenoxicam 0.2mg/kg IM vs morphine 0.2mg/kg IM	No	Tenoxicam: increase rescue morphine
Williams (2002)	Codeine 1.5mg/kg IM vs morphine 0.15mg/kg IM	Diclofenac 1mg/kg PR	Codeine: more rescue during first 2 and 4 hrs; no difference in pain scores

INTERVENTION: tonsillectomy + systemic analgesia (post meta-analysis)

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Antila (2006)	DB RCT (comp. generated) N=45 Age: 9-15yrs	T:tramadol 1mg/kg bolus +6hr infusion Ket: ketoprofen 2mg/kg bolus + infusion S: saline ALL: fent 3mcg/kg	VAS during swallowing (0-100) at 30,60,90mins & 2,6,24hrs PCA fentanyl	Ket: lower pain scores first 6hrs; decr PCA reqt 0-6hrs only; minor diff 24hr PCA No diff between T and S	Ket: higher bld loss intraop (vs placebo, no diff cf. T) No diff PONV	1- statistical rather than clinically significant diff
Hullett (2006)	DB RCT (?method) N=66 (28/32) Age: 1-8yrs	M: 0.1mg/kg morphine T: 2mg/kg tramadol ALL: oral paracetamol 30mg/kg; ondans; dexameth	PMH (local) pain score 0-10 Rescue	No diff pain scores or suppt analgesic reqt	Only one pt PONV Minor decr in episodes of desat at 1-2hrs postop but not other times	OSA patients
Alhashemi (2006)	DB RCT (computer rand.) Age: 3-16 yrs N=80	IV paracetamol 15mg/kg + IM saline OR IM pethidine 1mg/kg + IV saline ALL: fentanyl 1mcg/kg	Obj Pain Score (0-10) every 5 mins in PACU until discharge (40 mins) Rescue: morphine 50mcg/kg (OPS>5)	OPS not sign diff (ns) : one point lwr in pethidine grp (~2/10 vs 3/10) Rescue (ns) : 7/40 paracetamol; 0/40 pethidine	PONV (in PACU only): 3/40 both grps Ready for discharge: 15 vs 25 mins (paracet vs peth)	1- Inadequate power for difference in pain score Very short follow up (40 mins)
Ozalevli (2005)	DB RCT (consecutive "rand.") Age: 6-12yrs N=60	Postop PCA bolus M: 20mcg/kg morphine bolus (0.1mg/kg loading) T: 0.2mg/kg bolus (1mg/kg loading)	CHEOPS (0-10) 5,15,30mins and 1,2,4,6,24hrs	Pain scores : ns fist 60 mins; M:lower at 1,2 and 4hrs. PCA median dose M: 11.8mg(9.7-14); T:80mg(57-127)	Nausea score higher with M at 4,6,24hrs; nausea: T 3/30; M 11/30	1- inappropriate randomisation method

Keidan (2004)	DB RCT age 1.7-10yrs n= 60 day case	K: ketorolac 1mg/kg F: fentanyl 2mcg/kg ALL: paracet 30mg/kg PR; dexamethasone 1mg/kg (max 25mg); ibuprofen 10mg/kg postop	PONV : score 1=none to 4=multiple Objective Pain Scale every 30 mins until discharge Agitation postop; sleep pattern at home Parent at home: pain none, moderate, severe	No diff in pain score K: increased agitation in recovery No diff in vomiting High incidence behavioural change and sleep disturbance at home	No bleeding any grp	1- very high dose ketorolac; small numbers no difference
Sheeran (2004)	DB RCT Age >3 yrs (mean 7 yrs) N=45 (23/22)	R: rofecoxib 1mg/kg oral (max 25mg) P: placebo ALL: morphine 50mcg/kg; paracet 30mg/kg PR; dexameth 0.5mg/kg; ondansetron 0.1mg/kg	CHEOPS on arrival, before rescue (morph 25mcg/kg), and every 30mins in PACU; Wong-Baker faces on discharge and at rest and with swallowing (parent every 4hrs for 24hrs)	No difference : pain scores, PONV, PACU time or morphine	Parent – too few returned data – R: trend to lower pain score	1- Max CHEOPS or Faces score used to calculate diff b/w grps Small groups
da Conceicao (2006)	DB RCT (? method) N=90 Age: 5-7yrs	Saline (I) Ketamine 0.5mg/kg preop (II) or end of procedure (III) All: PR diclofenac 1mg/kg; dexameth, ondansetron	Oucher (0-100) every 20mins in PACU, 2hrly on ward Score >30 morphine 1mcg/kg(?) All regular paracetamol 20mg/kg	Decr pain scores with ketamine (no diff pre vs post) 1-8hrs; decr suppt analgesia	No diff in side-effects; only one pt PONV	1+ Sleep apnoea pts Very low dose morphine
Umuroglu (2004)	DB RCT (envelope method rand.) N=60 (15 per grp) Age: 5-12yrs	K: IV ketamine 0.5mg/kg M: IV morphine 0.1mg/kg T: IV tramadol1.5mg/kg S: IV N saline	Numeric Rating Pain Scale (NRS: 0-5, no-severe pain) & CHEOPS at 1,5,10,15,20,30, 45mins & 1,2,4,6hrs Time to first analgesic Intraop rescue: alfentanil Postop rescue: pethidine 1mg/kg in PACU, paracetamol on ward	Pain scores lower in M grp only at some time points Rescue analgesia: M 6/15; K 11/15; T 9/15, S 15/15 Time to first analgesic: longer in M grp	PONV: M 20%, T 20%, K 40%, S 6.6%	1+ very small sample size, wide variability in time to first analgesic high rate PONV

O'Flaherty (2003)	DB RCT age 3-12 yrs n=80 (20/20/20/20)	K: 0.15mg/kg; M: MgSO4 30mg/kg; K+M; P: placebo ALL: fentanyl 2mcg/kg; dexamethasone 0.2mg/kg	Objective Pain Scale (0-10) on arrival in PACU, 30, 60 and 120mins; fentanyl if OPS>4	OPS : no diff – tended to be low in all groups Trend to higher score and incr PACU analgesic use in placebo grp but not significant	No diff in vomiting; no bleeding any group. Dreaming in 3 receiving ketamine, 2 in no ketamine grps	1+ small sample groups
Elhakim (2003)	DB RCT (envelope method) N=50 Age: 5-12yrs	K: ketamine 0.1mg/kg IM OR placebo 20mins before All: preop PR diclofenac 2mg/kg; intraop fentanyl 1mcg/kg	Visual analogue (animal pics increasing size) 0-10 in PACU & 6,12,24 hrs CHEOPS at 30mins, 1,2,3hrs Nurse observer VAS at rest & drinking (6hrs) Time to first analgesia Rescue: morphine to 0.2mg/kg in PACU; rectal paracetamol 30mg/kg PRN	CHEOPS: K lower Rest (1.5vs2.5) & swallowing (3.5vs5) pain score at 6hrs: K Time to first analgesia: K 130 vs 84 mins Rescue in PACU: K 3/25 vs 9/25 Total paracetamol: lwr in K Oral intake: improved in K	PONV: no significant diff No reported psychomimetic effects	1- non-validated pain tool; not clear which pain scores reported in results table; improvement in swallowing and oral intake
Ozer (2003)	Observer blinded, randomised (?method) N=50 Age: 4-7yrs	T: tramadol 1mg/kg OR P: pethidine 1mg/kg	Bieri Faces Pain Scale (0-6) at 0, 10, 20, 45 mins in PACU Postop agitation: 1-3 (calm-hysterical)	Pain scores higher in T grp at 0,10,20mins (approx 2.5 vs 4/6) Agitation: T>P but not significant	PONV: T 2/25; P 3/25	1+ small sample size short follow up
Ewah (2006)	case cohort day stay tonsillectomy n=100 age: 2-14yrs	Protocol: PR diclofenac 1mg/kg; PR paracetamol 20mg/kg; IM codeine 1mg/kg; IV ondansetron 0.1mg/kg; dexamethasone 0.25mg/kg. Discharge meds: ibuprofen tds; paracet qds; codeine qds	Wong-Baker Faces (0-5) Rescue (score>2): oral ibuprofen 5mg/kg Q'airre telephone 3/7 after discharge (100% response rate)	Score 0-2: 88% before discharge Score 3-5: D1~18%; D2~20%; D3~16%	Vomiting: 0% before discharge; D1 7%; D2 3%	2+

White (2005)	Cohort following guidelines n=37 Retrospective grp of previous practice n=34	Protocol: oral paracetamol 20mg/kg preop; fentanyl 1-2mcg/kg IV; diclofenac 1-2mg/kg PR Discharge meds: paracetamol 15mg/kg 4/24; ibuprofen & codeine PRN	Oucher (0-100) and nausea score (0-4) 4 hrly until discharge	After guidelines: Intraop morphine 0 vs 3/34; early analgesia 16% vs 41% Additional ibuprofen 70% at 7.5hrs, 59% at 14hrs	After guidelines: vomiting 5%	2+ small sample sizes; paracetamol alone insufficient for analgesia postop

INTERVENTION: Tonsillectomy + LA						
AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SEC OUTCOME	EVIDENCE LEVEL / COMMENTS
Hollis (2000)	Meta-analysis Cochrane 6 trials	LA either injected before or after removal (5); spray after removal (1)	Pain score Supplemental analgesia	No significant difference	Small no. of trials and small sample sizes	1+
Naja (2005)	DB RCT age 5-12 yrs n=90 (30/30/30)	GA: no injection; S: GA+ saline injection; LA: GA+ 1.5mls (1ml 2%lig, 0.5mls 0.5% bup, 3.7mcg fent, 6.7mcg clonidine ALL: fentanyl 3-4mcg/kg	VAS 0-10 at 0,6,12 hrs and daily for 10 days Pain at rest, with jaw opening, with eating Oral intake first 10 hrs; Time to solids; cumulated analgesia	VAS lower in LA grp for first 4 days; LA<GA at day 10 (0.48 vs 0.10) LA: incr oral intake; incr proportion leave hosp within 24hrs (93 vs 60 vs 41%) Decrease postop analgesic reqt	Ear pain: LA 20%, S 46%, GA 52% Parent – incr proportion satisfied (90 vs 37 vs 14%)	1+Minor statistical changes in VAS after day 4 Saline injection alone increased surgical satisfaction and improved outcomes!
Park (2004)	DB RCT (computer generated) N=130 Age: 2-12yrs	Postop injection in tonsillar fossa 3mls S: saline OR R: ropivacaine 0.5% with adrenaline All: PR paracetamol 30mg/kg; fentanyl 1mcg/kg; dexamethasone 1mg/kg (max 25mg)	Obj Pain Score in PACU for 180 mins Time to oral intake Analgesic use (rescue: fentanyl IV, later oral paracetamol and codeine Follow up q'airre (day 1,3,7,14)	Pain scores: no sign diff first 120 mins No sign diff: time to oral intake; rescue analgesia; time to normal activity postop	R: worse behaviour score (minimal diff); incr PONV (41% vs 19%; ns); incr neck pain (day 1-14)	1+ authors' question if adequate sample size or benefit masked by fentanyl
Hung (2002)	DB RCT age 3-16 yrs n=99 (50/49) day case	S: saline B: bupivacaine soaked swabs in fossa after tonsil removed – no dose given ALL: diclofenac 1.5mg/kg	VAS Faces (1-6) at 1, 3, 6hrs; time to drink; time to eat; postop analgesia (paracet/codeine at home)	Decrease mean pain scores at 1,3,6hrs (eg.1.88±0.77 vs 3.12±1.88); decrease time to drink (104 vs 159mins); decrease time to solids (167 vs 194mins)	No diff in postop analgesic reqt Control: 2/49 admit for inadequate oral; 1/49 secondary haemorrhage	1+ statistical differences but relatively small ?clinical significance; groups too small for diff in side-effects
Giannoni (2001)	DB RCT age 3-15yrs	S:saline; R: ropivacaine 1% 0.15ml/kg; R+C: rop	VAS (0-10) at rest and drinking at day	Additional analgesia in recovery: S 21/21, R 15/21,	Ear pain: S 89%, R 63%, R+C 61%	1+

	n=64 (21/21/22)	+ clonidine 1mcg/kg peritonsillar injection pre-incision ALL: ibuprofen 15mg/kg + 1mcg/kg fentanyl	0, 1, 2, 3, 5, 10 Activity level (score 0-3) by parent Cumulative analgesia at day 3 and 5 (parac+codeine)	R+C 16/22 S: higher VAS in recovery – no diff at 24, 48 hrs – higher at day 3 and 5 VAS: no diff between R and R+C Cumulative analgesia: no diff at day 3, slight decr in R+C at day 5 (8 vs 11doses)	Earlier return to full activity: R+C 8.1 vs S 5.8 days No bleeding any grp	Mild improvement in recovery and at after day 3 VAS – same scale 0-10 for all ages VAS – lower for drinking than rest scores ?sensitivity
Kaygusuz (2003)	?blinded randomised (?method) n=80 Age: 6-14yrs	B: 0.25% bupiv with adr 3-5mls pre-tonsillectomy D: 1mg/kg dex in tonsil L: 10% lignocaine spray qds P: saline spray qds	VAS 0-5 4hrly for 1st day, then day 1,3,7	VAS: All grps (~2.5) < P (4.3): ns diff b/w grps Day 3: L < P; ns diff b/w other grps	PONV: no difference (8-10/20 each grp)	2-
Somdas (2004)	Cohort N=30 Age: 5-15yrs	Bupivacaine 0.5% tonsillar fossa on right and saline on left All: metamizole in PACU, paracetamol later	No pain, more on left, more on right, equal pain both sides: 1,4,8,16,24hrs	Pain didn't change on left, decreased at 8,16 and 24hrs on bupi side		2+ ?effect of LA injection only apparent after several hrs
Akoglu (2006)	DB ?method of rand N=46 (16/15/15) Age: 2-12yrs	Peritonsillar fossa inj pre removal 3-5mls B: bupiv 0.25% R: ropiv 0.2% S: saline All: preop oral paracetamol 20mg/kg; fent 1mcg/kg	mCHEOPS (0-10) 15mins & 1,4,12,16,24hrs; score>5 fent 0.5mcg/kg or paracetamol 10mg/kg	LA groups: decr pain score from 1-24hrs; decr suppt analgesia; incr time to first rescue	No diff in nausea or otalgia	1-

INTERVENTION: Strabismus or squint : LA / topical

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY	EVIDENCE LEVEL / COMMENTS
Steib (2005)	DB RCT Age: 2.5-6yrs N=40, 38 complete ?method of randomisation Surgery 35mins	Subtenon bupivacaine 0.5% vs saline before surgery by surgeon (2mls 2.5-4yrs; 3mls 4-6yrs) All: alfentanil 30mcg/kg + bolus 10mcg/kg if MAP increase 20% All: paracetamol 30mg/kg IV	CHEOPS pain scale (4-13) in recovery and every 30mins until discharge Rescue reqt: niflumic acid 20mg/kg PR score >6; nalbuphine 0.2mg/kg if high score persists	Intraop alfentanil*: 32.3±7.1 vs 43.8±11.5 Postop analgesic reqt for CHEOPS >6: NSAID* 12 vs 19 pts; nalbuphine* 0 vs 15 pts Decreased time in recovery*: 95±30 vs 145±47mins	Reduced OCR*: 4/35 vs 17/30 Reduced PONV*: nausea 0 vs 11; vomiting 1 vs 7 No block complications	1+ ? statistics incomplete pt numbers for pain scores – significant difference (9 vs 6) only at first and 30 minute time point (c/w titration of analgesia)
Deb (2001)	Not blinded, ?method of randomisation Age: 5-14yrs N=50 (strabismus 15/25 and 17/25) Surgery 65 mins	Peribulbar block by anaesthetist (0.3mg/kg 2%lig 0.5%bup mix) vs pethidine (1mg/kg) All: pethidine 0.5mg/kg if HR or BP >20% increase	Modified CHEOPS (0-9) at 30mins, 2 & 6hrs Pain score : colour scale (no, mild, moderate, severe) + VAS 0-10 at 2, 6, 24hrs Analgesic reqt: request or VAS>5 ibuprofen 10mg/kg in first 24 hrs	Intraop analgesia*: 0/25 vs 6/25 Increased proportion pain free at 30mins, 2, 6 and 24hrs Postop analgesic reqt: 6/25 vs 19/25 Parent satisfied*: 18/25 vs 5/25	Reduced OCR*: 1/25 vs 15/25 Reduced PONV*: 5/25 vs 19/25; severe (>3 vomits) 2/25 vs 10/25 No block complications	2+ Statistically but not clinically significant differences in intraop BP and HR Not blinded and inadequate control grp CHEOPS modified by grp – not validated
Sheard (2004)	Parents blinded Computer randomisation Age: 15yrs or	Subtenon lignocaine 1ml 2% lignocaine by surgeon at end All: codeine 1mg/kg PR,	Parental assessment of pain 30mins, 1,2,4hrs: Objective Pain	Pain score: *at 30 mins 6 vs 4; *total score over 4hrs 18.5 vs 22 Suppt analgesia: ns	No block complications	1- no injection in control grp; parental

	younger (6±3yrs) N=111 (54/57) Surgery majority bilat	diclofenac 1mg/kg or paracetamol 20mg/kg PR if asthmatic; ondansetron 0.1mg/kg; amethocaine 1 drop 1% at end	scale (4-12) Suppt analgesia: oral ibuprofen or paracetamol; IM codeine if severe (not req)	27/54 vs 23/57 (by nurses, not linked to pain score)		assessment only; summed pain scores (not valid, all due to difference at 1st measure); incomplete data
Chhabra (2005)	RCT (envelope) Postop assessor blinded Age: 3-15 yrs N=105 Surgery 40 mins	Peribulbar block (mix lig+bup by surgeon) vs fentanyl 2mcg/kg vs pethidine 1mg/kg All: IM ketorolac 1mg/kg	All India Pain Score at 2,6,24hrs Rescue: iv pethidine 0.5mg/kg or oral paracetamol 10mg/kg (which drug used not reported)	Time to first analgesic*: 7.1±1.8 vs 4.7±2 vs 1.8 vs 2.6 Number requiring suppt: ns	PONV (block vs peth*) : 1 vs 4 vs 9 (if present metoclopramide 0.15mg/kg) OCR: decreased by block (1 vs 8 vs 7)	1- ? pain score method and not clear who assessed primary aim was PONV not pain

* = significant difference; PONV = postoperative nausea and vomiting; OCR = oculocardiac reflex

Morton (1997)	Randomised (?method); ?blinded Age: 3-8yrs N=40 (18/17 analysed) Surgery 35 mins	2 drops oxybuprocaine 0.2% (shorter duration than amethocaine) vs diclofenac 0.1% after induction	Observer pain score (0-3) at wakening, 1,2,4,24 hrs Rescue: further eye drops; paracetamol 15mg/kg if pain persisted	Pain scores: 1 hr* 28% vs 71% no pain; other times similar Suppt analgesia: no differences (0-3 doses in 24 hrs)	PONV: ns differences OCR: no episodes in either group	1+ ?adequate sensitivity; no opioids & low rate PONV Day case: duration approx 30 mins
Kim (2003)	DB RCT Age: 2-7yrs N=51 (19/14/18) Anaesthesia time 60 mins	Amethocaine 0.5% vs ketorolac 0.5% vs saline: 2 drops at beginning and end of surgery All: dexamethasone 0.15mg/kg + perphenazine 35mcg/kg	CHEOPS every 5 mins in recovery Rescue: paracetamol 20mg/kg if pain score >6; codeine 1mg/kg second line (not req)	Pain scores: no sig. differences (mean 5 all groups) Analgesic requirement: ns (one dose paracetamol in 43%) Time to analgesic: ns (34 vs 57 minutes)	PONV: ns – rate low 2%' only recorded for first few hrs in hospital	1+ ?adequate sensitivity authors question if CHEOPS adequate for ocular pain inadequately powered for time to first analgesic
Bridge (2000)	DB RCT (?method of randomisation) Age: 4-12yrs N=30 (17/13) Surgery 25 mins	Ketorolac 0.5% vs saline: 6 drops at beginning and end All: paracetamol 20mg/kg preop	CHEOPS every 5 mins in recovery then Faces scale (Bieri 0-6) Rescue: morphine 20mcg/kg IV in recovery; codeine 0.5mg/kg oral later	Pain scores: no sig. diff. Time to first analgesic: ns Rescue: ns; morphine 7/17 vs 6/13, codeine 11/17 vs 7/13, paracetamol at home 13/17 vs 9/13	PONV: rate low; 3/17 vs 4/13 (some 24 hr data incomplete)	1+ ?adequate sensitivity authors question sensitivity/specificity of CHEOPS
Snir (2000)	Randomised (odd/even) Single blind Age: 8 ± 6 yrs N=40 Surgery: majority bilat (no time)	Diclofenac 0.1% vs dexamethasone 0.1% immediately postop and regularly for 4 wks	Discomfort: 0-3 (none-severe) at 1 day, 1,2 and 4 wks	Discomfort: lower score with diclofenac at 2wks (0.2±0.3 vs 0.6±0.5)	Conjunctival chemosis and IOP better with diclofenac	1- statistical but not clinical significant difference in discomfort score : predominantly surgical outcome study

Eltzschig (2002)	RCT (lottery randomisation) postop blinding only Age: 2-12yrs N=81 Surgery 75 mins	Remifentanil 1mcg/kg+ 0.1-0.2mcg/kg/min vs fentanyl 2mcg/kg+ 1mcg/kg every 45mins intraop All: PR paracetamol 10mg/kg	Objective Pain Score (0-10) at 15, 30, 45 and 60 mins postop Postop: score>3 PR paracetamol 10mg/kg, >5 oxybuprocaine drops	Higher pain scores for 30 mins with remi* (4.7 vs 2)	PONV: increased likelihood of early vomiting with fentanyl	1+ PONV primary aim

Wennstrom (2002)	Open Randomised (?method) Age: 4-16 yrs N=50 Surgery 40 mins	PR diclofenac 1mg/kg at induction vs IV morphine 0.05mg/kg at end of surgery All: oral paracetamol 15mg/kg preop; fentanyl 2mcg/kg at induction	Wong Baker Faces (0-5) every 3rd hr Rescue: morphine 0.05mg/kg IV (score >2) + 6/24 paracetamol 15mg/kg	Pain scores: no sig. diff. Suppt morphine: 5 vs 10pts	PONV*: 3/25 vs 18/25 Earlier discharge from PACU*: 240 vs 336 mins	2+
Shende (1999)	Blinded observer postop Randomised (assignment list) Age: 2.5-15yrs N=52 Surgery 50mins	ketorolac 0.9mg/kg IV vs pethidine 0.5mg/kg	Objective Pain Score on arrival, 30 and 60 mins in PACU Rescue: paracetamol 20mg/kg oral	Pain scores: no sig diff (all low, median 2) Suppt paracetamol: ns 10/26 vs 11/26	PONV*: 6/26 vs 19/26	1- pain scores low and only early assesst.
Mendel (1995)	Randomised (?method) Nurse assessor blinded Age: 1-10yrs N=54 Surgery 30 mins	ketorolac 0.9mg/kg IV vs fentanyl 1mcg/kg vs saline	Objective Pain Scale (0-10) 20,40,60 mins then hourly Rescue: score >2 paracetamol 10-20mg/kg PR; >5 IV fentanyl 0.5mcg/kg (not req)	Pain scores: no sig. diff. Suppt paracetamol: ns (13/18 vs 12/18 vs 14/18)	PONV*: 3/18 vs 13/18 vs 6/18	1- “pain scores low all groups” median 2-2.5 **full placebo group
Kokki (1999)	DB RCT (?randomisation	ketoprofen 1mg/kg + 1mg/kg over 2hrs vs	Maunuksela Pain score (0-10) 15 min	Pain score*: lower only at 30min time point	PONV*: 5/30 vs 12/29	1+

	method) Age 1-12yrs N=59 Surgery 30 mins	saline All: fentanyl 1mcg/kg	intervals, VAS in older children Rescue: fentanyl 1mcg/kg score >3	(correlation between observer and VAS reported scores) Suppt fentanyl: no. pts (21/30 vs 26/29) no sig diff; no doses* (44 vs 62) Time to first analgesic: no sig diff	Incr PONV associated with postop fentanyl, not with no. muscles or technique (recession vs resection)	
Mikawa (1997)	DB RCT (envelope method) Age: 2-11yrs N=90 Surgery 80mins	flurbiprofen 1mg/kg IV vs 0.5mg/kg vs saline	Objective Pain Scale on wakening then 30, 60, 90, 120mins, 3,4,5,6,8hrs Rescue: diclofenac PR 12.5 or 25mg if OPS>5	Highest OPS*: median lower with 1mg/kg, 4.5 vs 7.5 vs 7 Suppt diclofenac*: 15/30 vs 29/30 vs 28/30	PONV: ns 7/30 vs 9/30 vs 9/30	1+ Half-life 5.8hrs in adults Only max pain scores reported (?effect of time) **full placebo grp

INTERVENTION: Vitreoretinal surgery

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ 2^{o} OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Subramaniam (2003a)	Case control; randomised (?method of rand) N=85 Age: 6-13yrs	Peribulbar block IV pethidine 1mg/kg	4 point VAS (0,1,2,3) at 2,4, 24 hrs CHEOPS in PACU Rescue: peth 0.5mg/kg	LA grp: lower pain score in PACU; higher proportion pain free at all time points; decreased supplemental analgesia	Decreased incidence oculocardiac reflex and decr PONV with LA	2+ "pre-emptive" in title but not adequate design
Subramaniam (2003b)	DB RCT (random number table) N=86 Age: 7-16yrs	Ketoprofen 2mg/kg Pethidine 1mg/kg	4 point VAS (0,1,2,3) at 2,4, 24 hrs Rescue: score 2: oral ibuprofen; score 3:peth 0.5mg/kg	No significant diff in pain scores; no difference in rescue	PONV decr with NSAID	1-
Deb (2001) **also in strabismus	Case control; randomised ?method N=50 Age: 5-14 Strabismus (32); vitreoretinal (18)	Peribulbar block Pethidine 1mg/kg	Coloured 10 point VAS at 2,4, 24 hrs CHEOPS at 30 mins in PACU Rescue: oral ibuprofen (VAS>5)	Intraop analgesia*: 0/25 vs 6/25 Increased proportion pain free at 30mins, 2, 6 and 24hrs Postop analgesic reqt: 6/25 vs 19/25 Parent satisfied*: 18/25 vs 5/25	Reduced OCR*: 1/25 vs 15/25 Reduced PONV*: 5/25 vs 19/25; severe (>3 vomits) 2/25 vs 10/25 No block complications	2+ Statistically but not clinically significant differences in intraop BP and HR Not blinded and inadequate control grp CHEOPS modified by grp – not validated

INTERVENTION: Tympanomastoid surgery

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ 2^{o} OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Suresh (2002)	DB RCT (computer generated) N=40 Age: 2-18yrs cochlear implant (25), mastoidectomy (15)	Grt auricular nerve block 2ml 0.25%bupivacaine + saline IV Morphine 0.1mg/kg IV + saline block No other analgesia	Objective Pain Scale (OPS) every 5 mins for 60mins in PACU, then every 30 mins for 6 hrs Rescue (OPS>6) morphine 50mcg/kg	No significant diff : trend higher pain score and increase rescue with LA Pain at home: no diff in number of analgesic doses (77% return q'aire)	PONV : treat ondansetron : increased in opioid grp	1+ Power analysis based on PONV not analgesia; low numbers & high variability in pain scores
Suresh (2004)	DB RCT N=40 Age: 2-18yrs cochlear implant (23), mastoidectomy (17)	BB: grt auric nerve block bupi 0.25% before incision and 1/24 before end of case SB: saline before incision, bupi 1/24 before end of case No other analgesia	OPS every 5 mins for 60 mins in PACU then hrly for 6hrs Rescure (OPS>6): morphine 50mcg/kg	No significant diff: OPS, amount of rescue in PACU or during admission, time to first analgesia	PONV: no diff	1+ Aim to investigate pre-emptive effect
Hasan (2004)	Retrospective case series N=144 Age: 11±3.7yrs 45% middle ear, 55% mastoid	Anaesthesia and analgesia not standardised : intraop fentanyl	Pain: Wong-Baker (<8yrs); VAS (>8yrs)	Mastoid: increased likelihood to need morphine in PACU and require admission. Higher risk of PONV and require admission: cholesteatoma, pain score >5, morphine reqt in PACU	36% discharged same day; 92% discharged within 23hrs	2+

INTERVENTION: Dental procedures

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ 2^0 OUTCOME & CONCLUSION	EVIDENCE LEVEL / COMMENTS
Purday (1996)	DB RCT (?method of rand.; observer only blind) N=120 (30 each grp) Age: 2-10yrs Day case dental restorations (~50% extractions)	Ketorolac 0.75, 1, 1.5mg/kg Morphine 0.1mg/kg	Objective Pain Score 15 & 30 mins after arrival in PACU Rescue: paracetamol 20mg/kg or codeine 1mg/kg if OPS>6	No diff in pain score at 15 or 30 mins No diff in rescue or paracetamol doses at home first 24hrs	Increased vomiting in morphine grp; no bleeding problems	1- Brief follow-up Scores low in all grps with wide range (?sufficient power)
Littlejohn (1996)	DB RCT (?method of rand; observer only blind) N=60 (21/19/20) Age: mean 6yrs (minimum 2yrs) Day case extractions	IV nalbuphine 0.3mg/kg PR diclofenac 1-2mg/kg No analgesia	Objective Pain Scale (0-10) at 5,10,15,30,45 minutes after wakening Rescue paracetamol	No diff in pain scores, rescue or PONV		1- Very brief procedures : anaesth time <10mins Majority scores 0 (low sensitivity)
Roelofse (1999)	DB RCT N=60 Age: 4-7yrs Extractions (mean 10)	Oral tramadol 1.5mg/kg Placebo 30 mins preop	Objective Pain Scale; Oucher faces scale Rescue paracetamol	Oucher: significantly lower at 60 and 120mins Rescue 19.4% vs 82.8%	Longer recovery with tramadol (48 vs 36mins; wide SD both grps)	1- (abstract only)
Anand (2005)	Randomised: one side LA	Intraligamental LA to one side of mouth	VAS; rate which side better	VAS not significantly		2+ no control injection

	N=30 Age: 11.3±1.7yrs Extraction permanent molars			different between LA and contralateral side; 63% pain better on LA side (85% boys, 47% girls)		
Andrzejowski (2002)	DB RCT (envelope; observer only blind) N=120 Age: 5-12yrs Extractions >5 teeth	Soaked swabs over exposed teeth sockets Bupivacaine 0.25% + adr Saline All: PR diclofenac ~1mg/kg	4 point pain scale (0=don't hurt to 3=hurt the most): include non-validated cartoon faces 15 and 30 mins following recovery Nurse observer score	No diff in pain scores		1+
Gazal (2004)	DB RCT (computer generated envelope) N=135 Age: 2-12yrs Extractions (mean 7)	Soaked swabs over exposed teeth sockets Bupivacaine 0.25% + adr Sterile water All: oral paracetamol 15mg/kg preop	5 point distress scale (0-4) [faces scale similar to wong-Baker] Preop, immediate postop and 15 mins	No diff in "distress" scores	Increased distress <6yrs compared with older children irrespective of treatment group	1+ "decided to assess distress instead of pain because it can be difficult to measure pain in young children"
Greengrass (1998)	DB RCT (envelope) N=24 Age: 7-15yrs Extractions	Pain after extractions (24 of 42) randomised to soaked swab on socket: Bupivacaine 0.25% + adr Saline	?method "asked whether had pain or not"	Reduction in pain at 10 minutes in 10/12 of bupivacaine grp		1+ (abstract only)
Atan (2004)	Cohort: morbidity after day stay GA dental treatment N=121 Age: 6-16 Restorations 30%;	All: PR analgesia diclofenac, codeine, paracetamol ± alfentanil (no details of dose) 92% : LA during procedure	Anxiety and pain (Objective Pain Score in PACU and verbal scales): preop, before discharge, 36, 72 and 148hrs postop	OPS: 50% no pain in PACU LA reduced pain (OR 0.39) At 36hrs: 28% moderate and 9%	Increased pain associated with increased no. procedures.	2+

	extractions 60%; surgical procedure 54%			severe pain “Pain following dental GA was most prevalent and longlasting symptom of postoperative morbidity”		
Coulthard (2006)	DB RCT (computer generated) GA for dental extractions (1-10) N=142 Age: 4-12 yrs	2% ligonocaine with adrenaline OR saline buccal infiltration ALL: paracetamol 15mg/kg preop	Faces scale (not validated) by nurse on waking and 30 mins, parents at 24hrs	No difference in pain scores at waking, 30mins or 24hrs. No difference in proportion requiring paracetamol at home (doses not reported)		1- Limited assessment time points

INTERVENTION: Sub-umbilical surgery

h – inguinal hernia, o – orchidopexy, c – circumcision, hs – hypospadias, hc – hydrocoele, v – vur, p - phimosis

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Ivani et al., (2005)	RCTDB N=60 1-7yr h,o,c,hs	Caudal 1ml/kg 1. R0.2% 2. L0.2%	CHIPPS up to 24hrs Score>=4 paracet40mg/kg + codeine 1-2mg/kg	No difference pain scores Rescue analgesia Gp1(7) = Gp2 (6)	No difference motor block	1+
Willschke et al., (2005)	RCT N=100 0-8yr h,o,hc	IL/IG NB L0.25% 1. Ultrasound 2. Traditional 0.3ml/kg	Intraop – haemodynamics OPS – duration of block Score>11 paracet 40mg/kg pr	Gp 1 - ↓ intraop fentanyl and more stable haemodynaics. Also ↓LA use – 0.19ml/kg Gp 1 - ↓ paracet use (6 vs 40%)	Gp1 ↓ time of surgery (ns)	1+
Breschan et al., (2005)	RCT N=182 1-7yrs h,o	Caudal 1mg/kg 1. L0.2% 2. R0.2% 3. B0.2%	CHIPPS up to 24hrs Score>10 paracet 20-30mg/kg pr	No difference duration of analgesia, pain scores, analgesic use, No requiring no further analgesia (~1/3 in all gps)	No difference motor	1+
Martindale et al., (2004)	RCTDB N=30 3mn-6yr h,o	Caudal B0.25% 1ml/kg 1. Plain 2. +S-Ket 0.5mg/kg (caud) 3. +S-Ket 0.5mg/kg IV Paracet 20mg/kg po premed + diclofenac 1mg/kg pr indn	mOPS up to 24hrs score>4 Rescue analgesia Time to 1st analgesia	Gp2 ↑ Time to 1st analgesia, ↓ analgesic use in 24hrs No difference pain scores	No difference sedation, PONV, mictn, motor	1+
Leoni et al., (2004)	RCT n=82 0-8 YEARS MINOR ABDO	28 – alfent 25mcg/kg iv. 24 - periph nerve blockade with ropivacaine 0.475% 1ml/kg. 30 – 12.5 mcg/kg alfent iv + periph nerve blockade with	Intra op bp and pulse Post op FLACC obs tool + numerical scale done by nurses docs, parents and children	No difference intra or post op efficacy	No differences	1- no power calc. unequal groups suggests

	AND UROLOGICAL	ropivacaine 0.475% 1ml/kg.				poor randomisation technique
Ivani et al., (2003)	RCT N=60 1-7yr h,o,hc,hs,p	Caudal 1ml/kg 1. L0.125% 2. L0.2% 3. L0.25%	Intraop haemodynamics CHIPPS upto 24hrs Score>=4 paracet 40mg/kg + codeine 1-2mg/kg	Time to 1st analgesia Gp2=Gp3>Gp1 No difference use rescue analgesia	No PONV Minimal motor block in all gps	1+
Weber and Wulf, (2003)	RCTDB N=30 1mn -9yrs h,o,c,hc	Caudal B0.125% 1ml/kg 1. Plain 2. +S-Ket 0.5mg/kg	Intraop – haemodynamics OPS upto 24hrs Score>3 Paracet 20mg/kg pr	No further analgesia Gp2>Gp1 (10 vs3)	No difference motor, Haemodynamics No psychomotor effects	1+
Turan et al., (2003)	RCTDB N=44 1-6yr h,hs	Caudal R0.2% 0.5ml/kg 1. Plain 2. + Neo 2mcg/kg	Intraop – haemodynamics TPPPS up to 24hrs Score>3 paracet 20mg/kg pr Time to 1st analgesia	Gp2 - ↑ Time to 1st analgesia, ↓ pain scores at 6 & 12hrs, ↓ analgesic use, ↑pts requiring no analgesia (15 vs 4)	No difference PONV (low), sedation, motor	1+
(Surasera nivongse et al., (2003)	RCTB N=103 1-12yrs h,hc (2 exclusions analgesia for other reason)	Wound Infiltration vs IL/IG NB B0.5% 0.25ml/kg + Adr 5mcg/ml 1. Saline 20 – 60s pre closure 2. 20s pre closure 3. 60s pre closure 4. NB at induction	CHEOPS upto 24hrs Score>=7 fentanyl (hosp) paracet 10mg/kg (home)	Gp1 - ↑ pain scores, ↑ analgesic use, ↓ time to 1st analgesia No difference in other gps	PONV low in all gps 5pts in gp4 and 1pt in gp2 had temporary gait problems	1+
Ivani et al., (2002b)	RCTB N=60 1-7yr h,o,c,hc	Caudal 1ml/kg 1. R0.2% 2. B0.25% 3. L0.25%	Intraop – haemodynamics OPS up to 24hrs Score>=5 paracet 10-15mg/kg + codeine 0.5-1mg/kg pr	5pts in each gp required rescue analgesia No difference time to 1st analgesia	↓ motor in 1st hr in gp1 No difference haemodynamics	1+
Ivani et al., (2002a)	RCTB N=40 1-7yrs h,o	Caudal R0.2% 1ml/kg + Clon 2mcg/kg Vs IL/IG NB R0.2% 0.4ml/kg +	Intraop – haemodynamics OPS upto 24hrs Score>=5 paracet/codeine pr	Rescue analgesia gp2>gp1 (70 vs 45%) Time to 1st analgesia Gp1 160min vs Gp2 265min (ns)	No difference sedation	1+

		Clon 2mcg/kg				
Bosenberg et al., (2002)	RCTDB N=110 4-12yrs h,o,hc	Caudal 1ml/kg 1. R0.1% 2. R0.2% 3. R0.3%	Intraop – haemodynamics Faces + Observer 4pt scale up to 8hrs Score>3 or mod pain paracet 20-30mg/kg or tilidine 1mg/kg Time to 1st analgesia	No difference in time to 1st analgesia (3.3 vs 4.5 vs 4.2hrs) The higher the block the better the analgesia (ns) Pain scores and analgesic use ↑ Gp1 c.f. Gp3 In 1st 8hrs – 26pts in each gp needed paracet but dose↑ with ↓ Ropiv dose Tilidine use 18 vs 14 vs 11pts	Motor block: Gp3>Gp2>Gp1 No difference PONV (20-30%), mictn	1+
Ivani et al., (2000)	RCTDB N=40 1-7yr h,o,c,hc	Caudal R0.2% 1ml/kg 1. Plain 2. +Clon 2mcg/kg	Intraop – haemodynamics OPS up to 24hrs Score>=5 paracet 10-15mg/kg + codeine 0.5-1mg/kg pr	Time to 1st analgesia ↑ Gp2 (225 vs 125 min) Analgesic use ↓ Gp2 (2 vs 9) 5pts Gp1 needed analgesia in 1st 3hrs (0 in Gp2)	No difference motor, sedation, haemodynamics No PONV	1+
Kaabachi et al., (2005)	RCT N=98 1-12yr h,o	IL/IG NB B0.25% 0.3ml/kg 1. Plain 2. +Clon 1mcg/kg	CHEOPS 1-6yrs, VAS 6-12yrs upto 6hrs Score>6 or 50 paracet 15mg/kg iv Score 4-5 or 30-50 paracet 15mg/kg pr Parent questionnaire	No difference analgesic use, pain scores 3pts in each gp intraop fentanyl Over 6 days more pts in gp1 needed analgesia	No difference sedation scores	1-
Passariello et al., (2004)	RCTDB N=44 1-5yrs h,o,hc	Caudal 1ml/kg 1. S-Ket 1mg/kg 2. S-Ket 1mg/kg + Clon 1mcg/kg	Introp – haemodynamics CHEOPS Score>=9 Paract 200mg/kg + codeine 5mg/kg	No difference – time to 1st analgesia (16 vs 20hrs), pain scores Rescue analgesia Gp1 > Gp2 (38 vs 18%)	No difference mictn, motor, haemodynamics No PONV,	1-
Bano et al., (2004)	RCT N=60 1-8yrs ing + urogential	Caudal B0.25% 0.75ml/kg 1. Plain 2. +Midaz 50mcg/kg	Pain scoring(?) up to 24hrs Time to 1st analgesia Score>4 Diclofenac	↑ time to analgesia Gp2 (21.4 vs 9.9hrs)	↑ sedation in 1st hr in Gp2	1-
Joshi et	RCTDB	Caudal B0.125% 1ml/kg	Faces (hosp) – observational	No of patients needing fent > gp2	↑PONV gp2 (8 vs	1-

al., (2004)	N=36 6mn-6yr h,o,hc	1. Clon 2mcg/kg 2. Saline	Mod/severe – fentanyl VAS (home) Rescue – paracet/codeine	(9 vs 4) No difference time to 1st analgesia (3-4hrs) or analgesia at home	2)	
Khan et al., (2002)	RCTDB N=60 1-8yrs h,o Terminated at 30pts (10/gp) due to rate of PONV	Caudal B0.5% 2mg/kg 1ml/kg 1. Plain + IV saline 2. Plain + IV Buprenorphine 2.5mcg/kg 3. + buprenorphine 2.5mcg/kg + IV saline	Intraop – haemodynamics CHEOPS + VAS Score>4 or 30 – rescue analgesia Time to 1st analgesia	No further analgesics Gp3>Gp2>Gp1 (80 vs 50 vs 30%)	PONV Gp3>Gp2>Gp1 (80 vs 50 vs 20%)	1-
Luz et al., (1999)	RCT N=36 6mn-6yr h,o,c	Caudal B0.18% 1.5ml/kg 1. + Clon 1mcg/kg 2. + Morphine 30mcg/kg	Intraop – haemodynamics OPS upto24hrs Score>3 paracet 100-200mg or nalbuphine 0.2mg/kg	No further analgesia Gp1 61% Vs Gp2 50% Remaining pts no difference in analgesic use (1-3doses) OPS No difference and low in both gps	No motor, mictn, haemodynamics problems PONV 5 vs 4pts	1-
Bosenberg and Ratcliffe, (1998)	RCT N=88 2-10yrs h,o	1. IV Tramadol 1mg/kg 2. IV Tramadol 2mg/kg 3. IV Pethidine 1mg/kg 4. IV Saline	Intraop – haemodynamics 5pt verbal pain scale up to 6hrs Analgesic use	Pain scores Gp4>Gp3=Gp1>Gp2 Time to 1st analgesia: 218 vs 251 vs 223 vs 175min Pts needing rescue analgesia: 13 vs 9 vs 14 vs 15		1-
Gulec et al., (1998)	RCT N=60 1-12yrs h,o,c,hs,hc	Caudal B0.125% 0.75ml/kg 1. Plain 2. + Midaz 50mcg/kg 3. + Morphine 50mcg/kg	Intraop – haemodynamics 5pt pain scale – Verbal >5yrs, observational < 5yrs Score>=3 paracet 50-100mg/kg/day	Time to 1st analgesia Gp2>Gp3>Gp1 (21 vs 14.5 vs 8.1hrs)	PONV: Gp1=Gp3>Gp2 (30,35 vs 15%) Sedation: Gp2=Gp3>Gp1 No difference mictn, motor	1-

Anatol et al., (1997)	RCT N=183 5-12yr h,o,hc (15 exclusion lack of data or repeat procedure	B0.5% 0.4ml/kg 1. Infiltration 2. IL/IG NB 3. Combination	CHEOPS – up to discharge Score <=6 satisfactory, >=9 severe pain	No difference time to 1st analgesia, analgesic use (55-65%) Satisfactory pain – 78 vs 80 vs 81% Severe pain – 9.4 vs 8.4% vs5.9%	No difference PONV (~25%)	1-
Ho et al., (1997)	RCT N=51 1-6yr h,o,c	Caudal B0.25% 0.6ml/kg + Adr 1:200,000 1. Pre surg 2. Post surg	Faces pain scale (observational) Analgesic use	No difference between the groups		1-
Ivani et al., (1996)	RCT N=42 1-10yr h,o	Caudal Mepiv 1% 7mg/kg 1. + Saline1ml 2. + Clon 2mcg/kg	Broadman OPS	Time to 1st analgesia Gp2 >Gp1 (218 vs 143 min)	↑ sedation Gp2	1-
Dalens et al., (2001)	Cohort study N=22 1-12yrs h,hc	IL/IG NB R0.5% 3mg/kg	OPS up to 6hrs Score>4 paract 30mg/kg or nalbuphine 0.2mg/kg	Pain < 4: 73% at 1hr, 86% at 2hr, 91% at 3-6hr Mod/severe pain in 3pts at 1-2hr 9/22 needed rescue analgesia	1pt PONV 1pt Fem NB	2- 5pts given alfentanil
Lonnqvist et al., (2000)	Cohort study N=18 1-8yrs hs,o v	Caudal R0.2% 1ml/kg +paracet 100mg/kg/day	4pt pain scale upto 36hrs Time to 1st analgesia	90% pts good pain relief at all times Median time to 1st analgesia 12.6hrs	Vomiting 50% Pruritis 12% Motor block 0%	2-
Ho and Keneally (2000)	Case series N=90 1-13yrs h,o	Infiltration of IL/IG block – anaes dependent 2/3pts give paracet pr on indn	Pain scoring (?) in hosp Parent questionnaire at home Rescue paracet 15mg/kg or codeine 0.5 – 1mg/gk	More orchid patients required periop opioids and needed more paracetamol at home	PONV similar (20-30%)	3

INTERVENTION: Circumcision

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Allan *et al.* (2003)	Cochrane review 7 Studies 374pts 28dy – 16yr	Caudal vs DNB (2) Caudal vs opioid (4) Caudal vs opioid + paracet (1)	Rescue Analgesia (3) VAS scores (6)	Caudal vs DNB – No difference Caudal vs opioid - ↓rescue analgesia in early postop	No diff PONV ↓PONV with caudal	1+ - small no of studies, no firm conclusions
Weksler *et al.* (2005)	RCT N=100 3-8yrs	DNB B0.5% (+ aug) Vs Caudal B0.25% 1ml/kg	Intraop - haemodynamics Faces upto 2hrs Parent satisfaction + analgesia at home	No difference in any parameter	Caudal - ↑motor block and PONV	1+
Choi *et al.* (2003)	RCTDB N=60 2-12yrs	EMLA 2-4g + Saline DNB Vs DNB B0.5% 0.2ml/kg + placebo cream	Intraop – haemodynamics Cheops upto 6hrs Rescue analgesia (25%↑ haemo or score >5) – fentanyl + paracetamol	No difference in rescue analgesia either intra or postop.	No adverse effects	1+
Gauntlett (2003)	RCT N=60 1-10yrs	DNB B0.5% (+aug) Vs Caudal B0.15% 0.5ml/kg + Ketamine 0.5mg/kg	Parents OPS in hosp and at home Time to 1st analgesia (paracetamol)	No difference – time to 1st dose, no of doses and pain scores	↑ motor block and time to mict with caudal	1+
Lee and Sanders (2000)	RCTDB N=32 18mn – 12yr	Caudal 1ml/kg R0.2% Vs R0.2% + ketamine 0.25mg/kg (+Fent 1mcg/kg at indn both gps)	Parent VAS Time to 1st dose (4 on VAS) No of analgesics (paracet)	R+K - ↑ time to 1st analgesia - ↓ no of paracet doses in 24hrs	No diff – sedation, motor block, micturition, PONV	1+

McGowan *et al.* (1998)	RCT N=61 1-18yrs	1. DNB B0.5%0.3ml/kg 2. DNB + Diclofenac pr 2-2.5mg/kg 3. Diclofenac	CHEOPS upto 2hrs Questionnaire at home Rescue analgesia – morphine, paracet, lig gel	3 failed blocks Gp 3 ↑ pain score at 10min More paracetamol used (ns) Gp2 Less paracet over 2 days (ns) No difference – parental assessment	No difference bleeding /PONV	1+
Matsota and Papageorgiou-Brousta (2004)	RCT N=30 3-12yrs	Subcutaneous RB L0.25% Vs Fent 2mcg/kg + paracet 30mg/kg	Intraop – haemodynamics 4pt pain scale for 24hrs Time to 1st analgesia	↑ Haemodynamic stability with RB ↑ post op analgesia with RB (ns)		1-
Sharpe *et al.* (2001)	RCT N=74 1-9yrs	Caudal 0.5ml/kg 1. B0.25% 2. B0.25% + clonidine 1mcg/kg 3. B0.25% + clonidine 2mcg/kg	Intraop – haemodynamics Pain score (own) upto 4hrs, time to 1st analgesia, analgesic use	Trend toward ↑ time to 1st analgesia with↑ clonidine dose (ns) Low analgesic use and no difference	No difference sedation, micturiton, PONV (all low)	1-
Holder *et al.* (1997)	RCT N=45 3-11yrs	RB B0.25% Vs DNB B0.5% 0.2ml/kg	OPS upto 1hr Rescue analgesia – morphine/paracetamol /diclofenac	RB – 3 oedamatous - ↑ pain scores - ↑ morphine/paracet use		1- random allocation of rescue analgesia
Serour *et al.* (1996)	RCT N=250 6-17yrs	GA +DNB L2% + B0.5% 1ml/kg Vs DNB L2% + B0.5% 1ml/kg	Verbal Pain Score (own) Rescue analgesia	4pts in DNB needed GA GA group ↑ pain scores	GA - ↑ PONV and recovery time	1-
Irwin and Cheng (1996)	RCT N=50 2-12yrs	Caudal Vs RB	Time to 1st analgesia	Caudal - ↑time to 1st analgesia 8% RB failure	Caudal - ↑ time to micturition No difference motor block	1-
Taylor *et al.* (2003)	Open label N=22 5-24mn	Caudal L0.25% 0.8ml/kg	Intraop – haemodynamics Time to 1st analgesia – paracet 30mg/kg	All pts good intraop analgesia Time to 1st analgesia 7.9hrs	No adverse events	2+

			po/pr			
Soh *et al.* (2003)	Case series N=3009 1mn – 16yrs	DNB			9 complications Rate of 0.18% (excluding 2 drug errors)	3

INTERVENTION: Circumcision (neonates)

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Brady-Fryer *et al.* (2004)	Cochrane Review 35 Studies 1997 Newborns – term and preterm All RCT`s	DNB and/or RB (19 studies) EMLA/Lignocaine cream (12) Sucrose (9) Paracetamol (2) Environment manipulation (3) Either intervention vs placebo or intervention vs intervention All Awake	Haemodynamics Cry Pain scoring: NIPS, NFACS, PIPP + others Biochemistry	No study completely eliminated pain DNB, RB, EMLA, Lig > placebo DNB > RB > EMLA/Lig Sucrose, paracetamol, environment = placebo DNB – lower cortisol RB – oedema EMLA – results dependent on time of and success of aplication	No increased incidence of other side-effects with any procedure Using Mogen clamp ↓ duration of surgery	1++
Lehr *et al.* (2005)	RCT N=54 Term, <1week	Lig 4% vs EMLA vs DNB All Awake	Haemodynamic application, procedure, recovery	HR – no difference RR – EMLA > Lig = DNB	2 EMLA, 1 Lig – local reaction	1-
Taeusch *et al.* (2002)	RCT N=59 Term, neonate	DNB with lignocaine Mogen clamp Vs Plastibell All Awake	Length of procedure Behavioural score	Scores similar but: 70% DNB not fully effective 60% had “excessive” pain Plastibell procedure longer	Operators preferred Mogen Clamp	1-
Taddio *et al.* 1998)	Review 3 Studies 138 Neonates RCT`s	EMLA vs Placebo (2 studies) EMLA vs DNB vs RB vs placebo All Awake	NFACS Haemodynamics, Crying	DNB =RB > EMLA > placebo		1- (no stats)
Russell and Chaseling (1996)	Case series N=208 Neonates to 7 mn	EMLA preop All awake	Intraop behaviour Postop parent questionnaire	Little crying during procedure >90% settled rapidly postop, fed immediately, little pain at rest or on urinating	No serious complications	3

INTERVENTION: Hypospadias repair

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Mahajan *et al.* (2004)	RCTDB N=80 2-8yrs	Caudal 0.5ml/kg B0.25% 1. Plain 2. + Neo 2mcg/kg 3. + Neo 3mcg/kg 4. +Neo 4mcg/kg	Intraop- Haemodynamics OPS – if >3 the rescue analgesia – Paracet Time to 1st Analgesia	↑ time to 1st analgesia and ↓ analgesic consumption in Gps 2, 3 and 4	No difference PONV, sedation, motor block, haemodynamics	1+
De Negri *et al.* (2004)	RCTDB N=90 2-6yrs (9pts – failed block or change of surgery)	Epidural – intraop all pts R0.2% bolus → R0.125% infn Post op – infn 0.2mg/kg/hr 1. L0.125% 2. R0.125% 3. B0.125%	CHIPPS Score 4hly Score>4 rescue analgesia Time to 1st analgesia Analgesic consumption	No difference in pain scores, no rescue analgesia	No adverse effects	1+
Gunes *et al.* (2004)	RCT N=134 1-3yrs	Caudal vs IV Tramadol 1. C 2mg/kg post surg 2. C 2mg/kg pre surg 3. IV 2mg/kg post surg 4. IV 2mg/kg pre surg	OPS (Broadman) upto 24hrs Rescue analgesia – IV pethidine 1mg/kg or paracet 20mg.kg po	Duration of analgesia 1=2 >3=4 IV Peth: 0 gps 1& 2 but 30/34 gps 3 & 4 OPS↓ gps 1 & 2 at 3hrs	PONV: gp 1 6% other gps 40%	1+
Hansen *et al.* (2004)	RCTDB N=46 2-8yrs (2 exclusions – change surgery)	Caudal B0.25% 0.5ml/kg 1. + Clonidine 2mcg/kg C 2. + Clonidine 2mcg/kg IV Postop: P/NCA Morphine Bolus only (25ug/kg) and Paracet 20/kg 6hly po/pr	Intraop – haemodynamics Pain score – Obsevational (0-3) every 3hrs Score >1 – rescue morphine Time to 1st analgesia	No difference time to 1st analgesia, morphine use and pain scores (all low)	No difference sedation, PONV or motor block	1+
Batra *et al.* (2003)	RCTDB N=120 2-8yrs	Caudal 0.5ml/kg + adr 1:200,000 1. Neo 10mcg/kg	Intraop – haemodynamics OPS score > 3 paracet 20 mg/kg po	Gp 1&6 No diff but sig ↓ duration analgesia ↑ duration of analgesia as	Gp 4 & 5 ↑ PONV (upto 60%)	1+

		2. Neo 20mcg/kg 3. Neo 30mcg/kg 4. Neo 40mcg/kg 5. Neo 50mcg/kg 6. No Block	Time to 1st analgesia	dose ↑ (sin & ns) Gp 4 & 5 ↓analgeic consumption Gp 1 & 6 max analgesic use		
Abdulatif and El-Sanabary (2002)	RCT N=60 2-10yrs	Caudal 1. B0.25% 1ml/kg 2. B0.25% 1ml/kg + Neo 2mcg/kg 3. saline + Neo 2mcg/kg	Intraop – haemodynamics Pain score (0-10) – obs: score >4 paracet 15/kg Time to 1st analgesia	Intraop – gp 3 ↑RR, insp halothane Time to 1st analgesia ↑ gp 2 ↑ paracet usage gp 3 > gp 1 > gp 2	↑ PONV in gp 2 & 3 (~25%)	1+
Ozbek *et al.* (2002)	RCTB N=109 1-9yrs	Caudal 0.5ml/kg 1 Alfentanil 20mcg/kg 2 Ketamine 0.5mg/kg 3 Alfentanil 20mcg/kg + Ketamine 0.5mg/kg	Intraop – haemodynamics CHEOPS upto 24hrs Score >= 7 paracet 15/kg po Time to 1st analgesia	Duration of analgesia 3=2>1 1st 6 hrs – no use of analgesics and no difference pain scores Post 6hrs – Patients needing analgesia gp1 65% gp2 34% and gp3 33%	PONV 4pts in each group No difference mictn, motor, haemodynaics No psychomotor effects	1+
Prosser *et al.* (1997)	RCT N=90 13-53mns	Caudal 0.8ml/kg 1. B0.25% 2. Tramadol 2mg/kg 3. B0.25% + Tramadol 2mg/kg	Intraop – haemodynamics TPPPS – score >3 morphine 100mcg/kg or paracet 20mg/kg	↑ analgesic requirements and pain scores in gp 2	↑ PONV in gps 2 & 3 (ns)	1+
Chhibber *et al.* (1997)	RCTB N=99 6mn-12yrs (2 exclusions – surgical)	DNB B0.5% 1. 0.5ml/kg post surg 2. 0.5ml/kg pre surg 3. 0.25ml/kg pre & post surg	mOPS (0-6) at 15 min, 3,12 and 24hrs Pain → paracet 15ml/kg	Pain scores; all times gp 3 < gp 1, at 3 & 12 hrs gp 3 < gp 2, at 15 min gp 2 < gp 1 ↓ paracet use in gp 3 after 3hrs		1+
Kelleher *et al.* (1996)	RCT N=45 6mn-8yrs	Caudal B0.25% 0.5ml/kg 1. Plain 2. + diamorphine 30ug/kg	CHEOPS Time to 1st analgesia	↓ pain scores upto 30 min in gp 2 ↑ time to 1st analgesia in gp 2 (ns)	↑ PONV gp 2 (ns) ↑ time to mictn gp 2 (ns – most pts had catheter)	1+

Ozyuvaci *et al.* (2004)	RCT N=60 3-12yrs	Caudal B0.25% 0.5ml/kg 1. + paracet 20-25mg/kg pr with C 2. C alone 3. + paracet 20-25mg/kg pr at end	CHEOPS upto 6hrs Time to 1st analgesia	No difference pain scores or time to 1st analgesia		1-
De Mey *et al.* (2000)	RCTB N=60 8mn-13yrs	Caudal B0.25% 0.5ml/kg 1. Plain 2. + 1mck/kg clonidine 3. + 0.5mcg/kg sufentanil 4. + 0.5mcg/kg C + 0.25mcg/kg S	VAS if >5yrs CHEOPS if <5yrs 2hly upto 12hrs Score >40 or 6 paracet IV or PR	No difference pain scores or analgesic consumption	PONV – low in all groups	1-
Silvani *et al.* (2006)	Not Randomised N=30 1-5yrs	Caudal R 1.0.375% 0.5ml/kg 2.0.1% 1.8ml/kg	CHEOPS Time to 1st analgesia	↑ time to 1st analgesia and ↓ motor block in low concentration high volume group		2-

INTERVENTION: Orchidopexy

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Verghese *et al.* (2002)	RCT N=50 1-6yrs	Caudal B 2mg/kg + NaHCO3 0.1ml + Adr 1:400,000 1. 0.8ml/kg 2. 1ml/kg	Intraop-haemodynamics Analgesic consumption	Response to cord traction Gp1 65% vs Gp2 30% 4 vs 2 pts needed rescue analgesia	No difference motor block	1+
Findlow *et al.* (1997)	RCT N=40 2-7yrs (4 excluded – 2no surgery & 2 no follow up)	Caudal B0.25% 1ml/kg + ketamine 0.5mg/kg Vs IL/IG NB B0.25% 0.5ml/kg + Infiln B0.25% 0.5ml/kg (at end) Diclofenac 1-2mg/kg PR (both gps)	Parental OPS – 24hrs Score>4 – paracet 15mg/kg po Time to 1st analgesia and analgesic use	Time to 1st analgesia ↑Gp1 (10 v 3hrs) ↓ analgesic use Gp1 Gp 2 14 vs Gp 1 7 - Needing 2 or more analgesic doses	No difference sedation, motor, mictn, PONV (only 1 pt) No psychomotor effects	1+
Semple *et al.* (1996)	RCT N=60 1-9yrs	Caudal B0.25% 1ml/kg 1. Ketamine 0.25mg/kg 2. Ketamine 0.5mg/kg 3. Ketamine 1mg/kg	Parental OPS for 24hrs Score>4 paracet 15mg/kg	↑Time to 1st analgesia with ↑ Ketamine – Gps 3 & 2 vs Gp 1 (sig) ↑ Analgesic requirement Gp1 vs Gp 3 (sig) and Gp 1 vs Gp 2 (ns) No difference pain scores up to 4hrs	No difference mictn, motor, sedation PONV ↑ with ↑ Ketanine but (ns) Gp 3 - 7pts short lived psychomotor effects	1+
Somri *et al.* (2002)	RCT N=30 1-8yrs	Caudal B0.25% 1ml/kg Vs IL/IG NB B0.25% 0.5ml/kg + Infiln B0.25% 0.25ml/kg (at end)	CHEOPS upto 1hr Score >5 – fent 1mcg/kg or paracet 15mg/kg Stress Hormones	Gp 2 - ↑ pts needing fentanyl & more given (ns) No difference time to 1st analgesia and paracet use	↓Ad & Norad levels in caudal group post block insertion	1-
Johnston *et al.* (1999)	RCT N=40 1-5yrs	Caudal 1ml/kg 1. B0.125% + 0.5mg/kg Ketamine 2. B0.25% + 0.5mg/kg	Parental OPS for 24hrs Score > 4 – paracet 15mg/kg po	Gp 2 ↑ time to 1st analgesia – 9.5 vs 8 hrs (sig) No difference in median No of paracetamol doses (=2)	No difference motor block, mictn, eye opening No psychomotor	1-

		Ketamine Diclofenac 1mg/kg PR at induction (both groups)			effects	

INTERVENTION: Inguinal Hernia

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Yildiz *et al* (2006)	RCT N=60 1-10yrs	Caudal B0.125% 1ml/kg 1. Plain 2. + Clonidine 1mcg/kg 3. + Clonidine 1.5mcg/kg 4. + Clonidine 2 mcg/kg	Intraop – haemodynamiccs mCHEOPs or VAS painscale. Paracetamol if mCHEOPS > 5 or VAS > 30mm Time to 1st analgesia	↑ Time to 1st anangesia with clonidine 2mcg/kg	No ↑ in side-effects with ↑clonidine dose	1+
Kumar *et al.* (2005)	RCTDB N=80 5-10yrs	Caudal B0.25% 1ml/kg 1. Plain 2. + Midaz 50mcg/kg 3. + Ketamine 0.5mg/kg 4. + Neo 2mcg/kg	Intraop – haemodynamiccs 5pt Verbal pain score for 24hrs Score>5 paracet 20mg/kg po Time to 1st analgesia	Time to 1st anangesia: Gp 2 = Gp4 > Gp3 >Gp1 (sig)	No difference PONV, sedation, neurological outcome, motor block 2pts with ketamine had hallucinations	1+
Panjabi *et al.* (2004)	RCT N=60 6mn-10yrs	Caudal B0.25% 0.75ml/kg 1. + Ketamine 0.25mg/kg 2. + Ketamine 0.5mg/kg 3. + Ketamine 1mg/kg	Intraop – haemodynamics AIIMS pain scale up to 24hrs Score>4 peth IM 1mg/kg Time to 1st analgesia	Time to 1st anangesia: Gp 2 = Gp3 > Gp1 (sig) Supplementary analgesics – Gp1 90%, Gp 2 20% and Gp 3 0%	No difference sedation, motor block, mictn, PONV Behaviour effects Gp3 9, Gp2 1 and Gp1 0	1+
Machotta *et al.* (2003)	RCT N=58 0-5yrs	Infiltration B0.5% 0.2ml/kg post surg Vs Caudal B0.25% 1ml/kg	OPS upto 24hrs Score>5 – piritramide 0.05mg/kg iv, paracet upto 100mg/kg/day	No difference use piritramide in recovery (11 vs 8) or paracet use on ward (10 vs 7) No difference pain scores at any time except 2hrs when lower with caudal		1+

Memis *et al.* (2003)	RCTB N=45 1-5yrs (2 exclusions – analgesia for other reason)	Caudal B0.25% 0.5ml/kg 1. Plain 2. +Neo 1mcg/kg	Intraop – haemodynamics TPPPS score upto 24hrs Score>3 paracet 20mg/kg pr	No difference duration of block (15hrs – wide variation), those not needing any rescue (14 vs 15)	No difference PONV (1 vs 3), sedation, motor, haemodynamics	1+
Baris *et al.* (2003)	RCTDB N=78 6mn-6yrs	Caudal B0.25% 0.75ml/kg 1. + fent 1mcg/kg 2. + midaz 50mcg/kg 3. plain	Intraop – haemodynamics CHEOPS for 24 hrs Score>5 paracet 20mg/kg pr	No difference pain scores (all low) or analgesic use (7 vs 8 vs 5)	No difference mictn, motor, PONV (low) or haemodynaics	1+
Ozcengiz *et al.* (2001)	RCTDB N=120 4-10yrs (4 exclusions Unable to place block)	Caudal 0.5ml/kg 1. Tramadol 2mg/kg pre surg 2. Morphine 30mcg/kg pre surg 3. Morphine 30mcg/kg post surg	Intraop – haemodynamics OPS upto 24hrs Score>5 morph 0.1mg/kg IM	>90% pts in all gps – no further medication 8pts needed morphine (3 vs 3 vs 2)	No diff haemodynamics, PONV, sedation, puritis ↑ sevo use gp3	1+
Koinig *et al.* (2000)	RCTDB N=42 1-7yrs	Caudal S-Ket 1mg/kg Vs IM S-Ket 1mg/kg	Intraop – haemodynamics OPS upto 24hrs Score>11 paracet 20mg/kg pr Time to 1st analgesia	Time to 1st analgesia - ↑ caudal Analgesic use 12/22 caudal vs 18/20 IM (sig) ↓pain scores caudal at 75 & 90min	No difference sedation, mictn, haemodynamics	1+
Marhofer *et al.* (2000)	RCTDB N=49 3mn-6yr	Caudal 0.75ml/kg 1. B0.25% + Adr 1:200,000 2. S-Ket 0.5mg/kg 3. S-Ket 1mg/kg	Intraop- haemodynamics OPS up to 6hrs Score>11 paracet 30mg/kg/pr	Time to 1st analgesia Gp1 =Gp3 >Gp2 Analgesic use Gp1 30% = Gp3 33% < Gp2 72%	No difference haemodynamics, sedation, mictn	1+ But only 6hrs
Gaitini *et al.* (2000)	RCTB N=60 1-8yrs	Caudal B0.25% 1ml/kg 1. Plain 2. + Fent 1mcg/kg	Intraop – haemodynamics CHEOPS upto 12hrs Score>5 fent1mcg/kg or paracet 15mg/kg po Time to 1st analgesia	No difference - time to 1st analgesia or pain scores (lower in gp2 but ns) Rescue analgesia – fent 5 vs 6, paracet 14 vs 12	No difference PONV (3vs4), sedation, catecholamine levels	1+

Koinig *et al.* (1999)	RCTDB N=57 1.5-7yrs	Caudal 0.75ml/kg 1. B0.25% 2. R0.25% 3. R0.5%	Intraop- haemodynamics OPS up to 24hrs Score>11 paracet 20mg/kg pr Time to 1st analgesia	Time to 1st analgesia Gp3 > Gp1=Gp2 (large diff) Analgesic use Gp3 < Gp1=Gp2 Pain scores at 3,4hrs Gp3 < Gp1=Gp2	Time to mictn, standing ↑ Gp3	1+
Kundra *et al.* (1998)	RCTDB N=60 9mn-12yr	Caudal B0.25% 0.66ml/kg + Morphine 0.02mg/kg 1. 15min pre incision 2. Post surgery	Intrao – phaemodynamics OPS up to 24hrs Score>=5 morphine 0.1mg/kg IM Analgesic use	OPS ↓ in Gp1 at all times (sig at 0.5, 4 & 8hrs) Time to 1st analgesia ↓ Gp1 Morphine use ↑ Gp2	No difference PONV	1+
Klimscha *et al.* (1998)	RCTDB N=58 6mn-6yr	Caudal B0.25% 0.75ml/kg 1. Plain 2. +3.75mcg/kg Adr 3. +1mcg/kg Clon 4. +2mcg/kg Clon 5. Placebo	Intraop – haemodynamics OPS upto 24hrs Score>11 paracet 15mg/kg pr Time to 1st analgesia	In 1st 6hrs – Time to 1st analgesia: gp3=gp4 > gp1=gp2 > gp5 Analgesic use: all in gp5, gp3=gp4 < gp1=gp2 18hrs at home: Analgesic use: gp3=gp4 < gp1=gp2=gp5	No difference PONV, motor	1+
Naja *et al.* (2005)	RCT N=50 5-12yr	GA/PVB – mixture Lig2% + Lig2% with Adr 1;200,000 + Fent + Clonidine Vs GA/Fentanyl	Intraop – haemodynamics VAS score – nurses then parents upto 48hrs Score>5 - tramadol, paracet if child/parent request	GA/PVB – stable haemodynamics intraop, lower pain scores	PVB – leave hosp earlier, ↑ surgeon and parent satisfaction	1-
Sasaoka *et al.* (2005)	RCT N=100 6mn-10yr	II/IG NB B0.25% 0.75ml/kg 1. Alone 2. + GenitoFem NB B0.25% 0.375ml/kg	Intraop – haemodynamics Pain score (?) upto 5hrs Rescue – Diclofenac 1mg/kg pr	↓ HR/BP on sac traction in Gp2 No difference pain scores and rescue analgesia		1-
Sakellaris *et al.* (2004)	RCT N=45 6-10yrs	Infiltration R0.5% 0.25ml/kg 1. Pre surg 2. Post surg 3. No infiltration	OPS Paracet on demand Cortisol/prolactin levels	Time to pain score=0 ↓Gps 1 & 2	Gp 3 - ↑ postop cortisol and prolactin levels	1-
Gunes *et al.* (2004)	RCTDB N=99	Caudal 0.5ml/kg 1. R2mg/kg	Introp – haemodynamics CHEOPS then parental	Time to 1st analgesia: Gp3 > Gp2 > Gp1 (ns 16-23hrs)	PONV Gp1 (1) > Gp2 = Gp3 (7,8)	1-

	1-10yrs	2. R1mg/kg + Ketamine 0.25mg/kg 3. R1mg/kg + tramadol 1mg/kg	assessment up to 24hrs Score>7 paracet 15/kg po Time to 1st analgesia	Gp3 > Gp1 (sig) Analgesic use Gp1 = Gp2 (14, 11) > Gp3 (3)	No difference motor, haemodynamics, sedation	
Tsuchiya *et al.* (2004)	RCTB N=30 1-8yrs	IL/IG NB 0.5ml/kg 1. R0.2% 2. B0.25% 3. Lig1%	FACES by parents at 2 & 6hrs Pain – paracet 50 – 100mg pr	Pain scores at 2 & 6hrs Gp3 > Gp1=Gp2 Analgesic use Gp1 1, Gp2 1, Gp3 3 (ns)	No PONV, motor	1-
Schrock and Jones (2003)	RCTB N=54 1-6yr	Caudal B0.175% + Adr 1:200,000 1. 0.7ml/kg 2. 1ml/kg 3. 1.3ml/kg Paracet 30mg/kg PR indn (all gps)	CHEOPS in hosp, Parental VAS at home up to 24hrs Time to 1st analgesia Rescue analgesia – fent, oxycodone (hosp) paracet, codeine (home)	No difference Time to 1st analgesia (3.5-5hrs) CHEOPS no difference and low Recovery analgesia – 4 vs 3 vs 1 (ns) 36 pts analgesed at home – no diff between gps and no consistency with parental decision	No difference mictn, motor	1-
Hager *et al.* (2002)	RCTB N=53 1-72mn	Caudal 0.75ml/kg 1. Ket 1mg/kg 2. Ket 1mg/kg + Clon 1mcg/kg 3. Ket 1mg/kg + Clon 2mcg/kg	Intraop – haemodynamics OPS up to 24 hrs Score>11 paracet 30mg/kg pr Time to 1st analgesia	Time to 1st analgesia – Gp2=Gp3>Gp1 Analgesic requirement – Gp2=Gp3 > Gp1 (16% vs 63%)	No difference mictn, haemodynamics No adverse effects	1-
Lim *et al.* (2002)	RCT N=90 2-12yrs (5 exclusion Failure tech, poor anat, data lost)	IL/IG NB B0.25% 0.25ml/kg 1. Single shot 2. Double shot Post discharge paracet 10mg/kg po 6hourly (both gps)	Intraop – haemodynamics mCHEOPS up to 24hrs score4-5 paracet 15mg/kg po score 6 paracet + fent 1mcg/kg	Success rate 72% (both gps) No difference analgesic use 50% children pain in 24hr period		1-
Senel *et al.* (2001)	RCT N=60 1-7yrs	Caudal 1ml/kg 1. B0.25% 2. B0.25% + Tramadol	Intraop – haemodynamics 3pt pain scale up to 24hrs Score>1 paracet 10mg/kg	Time to 1st analgesia gp2 (13.5hr) > gp1 (9.8) > gp3 (4.7) (sig) Gp3 - ↑ rescue analgesia + pain	No difference RR, sedation, PONV (low), mictn, motor	1-

		1.5mg/kg 3. Tramadol 1.5mg/kg	pr Time to 1st analgesia	scores at 4 & 6hrs		
Hashizume *et al.* (2001)	RCT N=60 1-5yrs	Caudal 1mg/kg 1. Mepivacaine 1% 2. B0.25% 3. M 1% + B0.25% (50:50)	OPS up to 24hrs Score>3 paracet 20mg/kg pr	Low use of postop analgesia 4 vs 0 vs 0		1-
Joshi *et al.* (1999)	RCT N=56 6mn-6yrs	Caudal 1ml/kg + Adr 1:200,00 1. B0.125% 2. B0.125% + Fent 1mcg/kg 3. B0.25% 4. B0.25% + Fent 1mcg/kg	OPS in recovery VAS at home by parent or child Rescue paracet/codeine	No difference pain scores, analgesics at home 21% pts received IV fent (?when and why) – more in Gp1		1-
Splinter *et al.* (1997)	RCTB N=164 2-6yr	Infiltration + direct vision IL/IG NB B0.25% 0.2ml/kg (surgeon) 1. Caudal B0.2% 1ml/kg + Adr 1:200,000 2. Ketorolac IV 1mg/kg	mCHEOPS up to 24hrs score>5 morphine 50mck/kg or paracet 15/kg or codeine 1mg/kg	No difference pain scores in recovery ↓pain scores at home Gp2 Up to 2 hrs – paracet (59 vs 61) and codeine (56 vs 50) use no difference	PONV, motor and mictn all ↓Gp2	1-
Dahl *et al.* (1996)	RCTDB N=50 2-10yr	Infiltration 1. B0.25% 1ml/kg pre + saline post 2. Saline pre + B0.25% 1ml/kg post Paracet 15-20mg/kg pr on admission to recovery (both gps)	OPS + questionnaire	↓score at 30min Gp1 No difference post op analgesia Postop opioids 54% vs 45%		1-
Taylor *et al.* (2003)	Open label N=27 5-24mn	Caudal L0.25% 0.8ml/kg	Intraop – haemodynamics Time to 1st analgesia – paracet 30mg/kg po/pr	22/27 pts good intraop analgesia Time to 1st analgesia 7.34hrs	No adverse events	2+
Kokki *et al.* (2000)	Open label N=190 6mn-10yrs	Spinal B0.5% 0.3-0.4mg/kg + IL?IG NB B at end of procudre + either ketoprofen 2mg/kg IV or Ibuprofen 10mg/kg pr or paracet 40mg/kg pr	Maunuksela pain scale Score>3 rest or >5 activity fent 1mcg/kg Parent questionnaire	183 successful – 2 GA, 7 sedation 28% fentanyl in recovery 83% pain at home (17%mod, 2%severe) 85% analgesia at home, median 4 doses	7% PONV 6% headache	2+

Brindley *et al.* (2005) incarcerated hernia	Retrospective review N=12 2-17wk	Awake Cuadal B0.25% 1ml/kg		All successfully reduced	No adverse events	3

INTERVENTION Fundoplication

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Lejus (2001)	Prospective evaluation of epidural over 6 years. N=348 (307 children 12 days to 18 years, median 72 months)	Bupivacaine (mean concentration 0.185%)and Fentanyl (5ug/kg/day). Different types of surgery including fundoplication.	Hourly pain scores (Krane et al) Global pain index	Combination provides safe analgesia	Urinary retention 17% N & V 14% Pruritus 0.6%	3 prospective but not analytical
Wilson (2001)	Retrospective review Non random allocation N=104 (65 epidural, 39 infusion)	Epidural (bupivacaine/fentanyl mixture 0.125% at 0.4ml/kg/hr) v morphine infusion (10-40ug/kg/hr)	Hourly Pain measurements routinely performed. Need and duration of icu stay. Hospital stay M & M	Hospital stay greater for opioid group (13 v 8)	Mean duration of stay higher in opioid group. Patients in hospital more than 7 days higher in opioid group	3 case series
Dick (1998)	Prospective non randomised (but blinded for data collection) N= 40 (20 open, 20 lap)	Assessment of morphine usage post op	Duration and amount of morphine given. Linear pain scale	Equal amounts of morphine given (0.432+/-0.28, o.427+/- 0.28 mg/kg) More morphine required day 1 for lap procedure (0.399 +/- 0.19 v 0.22 +/-0.11. p< 0.03) But shorter time in lap group 1.2+/-0.46, 2.7+/- 0.67 days p<0.02. Similar amounts of NSAID given		2- non randomised. no primary end point or calculation of power. Different surgeons performed open and lap procedures.

Brenn (1998)	Prospective data acquisition. non-randomised 92 patients Mean age 107 months Orthopaedic and upper GI surgery	First 44 - bolus epidural morphine (caudal or lumbar) Subsequent 48 – post op continuos bupivicaine (0.2 – 0.5 ml/kg/hr 0.1%) and fentanyl (2mcg/ml)	CHEOPS used for analgesia. Incidence of complications. Comparison of di and quadroplegia	Vomiting seen more in diplegic group ($p<0.01$) Pruritus higher in diplegic group ($p<0.0002$) Neither of above related to mode of analgesia. Incidence of sedation higher in bolus group ($p<0.01$)	Bupivicaine and fentanyl better than opioid	3 non randomised
Rowney (2000)	Retrospective review N=51 Laparoscopic Nissen Median age 6yrs (5 months – 20 yrs)	Multi modal technique Port infiltration with 0.25% bupiv + 1 in 200 000 adrenaline Intra op fentanyl (2mcg/kg/hr) +rectal NSAID (34 patients) and rectal para (36 patients). Morphine infusion (first 4 patients). IM morphine 100mcg/kg given at end of surgery (24 patients). IM codeine (1mg/kg) in 20 patients.	No formal pain scores or charting. Assessment by nurses and anaesthetists	No post op analgesia required in 34 patients after 24hrs. No post op analgesia required in 45 patients after 48hrs.		3 not analytical. no historical control.
Mcneely (1997)	Retrospective review N=155 1 month to 19 years elective open fundoplication	bolus iv morphine N=91 (0.05 – 0.1mg/kg 1-2 hrly) v epidural N=72 (0.25% bupiv intra-op + fentanyl or morphine with 0.0625 – 0.125% bupiv	Post op course (analgesic efficacy, complications, hospital stay, cost) Pain via VAS or observational scale (Oucher)	Decrease complications in epidural group (decrease ventilation ($P<0.01$), shorter hospital stay ($P<0.01$), cheaper ($P<0.01$))		3 not analytical. only patients in epidural group managed by specific pain service

INTERVENTION Appendicectomy

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Jensen (2004)	DB RCT N = 68	B O.25% or 0.5% (>40kg<) or placebo 0.5 ml/kg sub cut	Morphine usage in first 24 hours	B 0.065mg/kg P 0.073mg/kg Ns	B group experienced longer pain relief (ns)	1+
Yildiz (2003)	RCT non blinded N= 40 (20 in each group) Age range 6 – 15	pethidine load (0.3 mg/kg then 150mcg/kg bolus iv. Pethidine load (0.3mg/kg then 75mcg/kg bolus + 15mcg/kg/hour background Lock out 20 mins in both	Pain Sedatiuon nausea in first 24 hours (4 point scale for each)	No difference between groups Background group had lower peth consumption in first 24 hours ($p<0.01$)	No significant side effects	1- no specific end point or power calculation
Dix (2003)	RCT non blinded N=75 Age 7-16 years	All had pca morphine + para +NSAID a) saline infusion b) Ketamine 500mcg/kg iv iv pre incision + saline infusion c) Ketamine 500mcg/kg iv iv pre incision + ket infusion 4mcg/kg/min postop	Primary - Morphine consumption at 24hrs Secondary - Rescue analgesia Side effects Satisfaction scores	No difference in morphine consumption in the groups Ket infusion required more doses of rescue and reported more side effects (hallucinations)		1+ envelope randomisation.
Munro (2002)	RDBT N=60 (53 completed) 5 – 13 years	Control (no intra or post op antiemetic) Ondansetron 0.1mg/kg (intra op + added to post op PCA) Droperidol 0/01mg/kg (intra op + added to post op PCA) All had morphine PCA (20mcg/kg bolus at 5 min lock out with background of	Pain (method not stated) Nausea Vomiting Sedation First 24 hours	No sig difference in PONV and sedation scores		1- unclear power calculation. low group numbers.

		4mcg/kg/hour)				
Wright (2001)	DBRCT N=60 (52 completed)	Wound infiltration Either bupivicaine or placebo	Post op pain assessed by child, recovery sister, ward sister Time to first narcotic injection	Significant decrease in pain in bupivicaine group		1+ sample size seems low
Morton (1999)	RCT non blinded N=80 (20 in each group) 5-13 years	Pca morphine 20mcg/kg bolus then 4mcg/kg/hr background for 12 hrs. Morphine + diclo 1mg/kg 8hrly. Morphine + para 15-20mg/kg 6hrly. Morphine + diclo and para. All had wound infiltration with 0.25% bupiv 1mg/kg	Morphine consumption Analgesia (3 point pain score) 3 point nausea score 3 point sedation score	Morphine consumption reduced by diclo ($p<0.0033$ for MD and $p<00.28$ for MDP). Para not additive ($P<0.144$).	Analgesia effect significantly improved by diclo despite lower morphine consumption	1+ Equal in groups Duration of pca equal
Habre (1999)	Case report N=2(10 and 8 yrs)	Addition of droperidol to morphine infusion Doses 0.14mg/kg and 0.17mg/kg	Symptoms at 38 and 27 hours	Extrapyramidal side effects		3

INTERVENTION Laparoscopy

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Borkar (2005)	Randomisd non blinded N=50 3 – 13 years. laparoscopic procedures	1. caudal Bupivacaine 0.2% 1mg/kg 2. diclo supp 3mg/kg + Bupivacaine 0.5% port site infiltration at end of procedure	Hannallah objective PS 15,30,60,120 and 360 mins	Comparable pain scores at all times	12% G1 and 20% G2 required rescue (ns)	1- no power calc. no mention of randomisation method.

INTERVENTION Abdominal surgery

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Leoni (2004)	RCT N=82 0-8 YEARS MINOR ABDO AND UROLOGICAL	28 – alfent 25mcg/kg iv. 24 - periph nerve blockade with ropivacaine 0.475% 1ml/kg. 30 – 12.5 mcg/kg alfent iv + periph nerve blockade with ropivacaine 0.475% 1ml/kg.	Intra op bp and pulse Post op FLACC obs tool + numerical scale done by nurses docs, parents and children	No difference intra or post op efficacy	No differences	1- no power calc. unequal groups suggests poor randomisation technique
Klamt (2003)	RCT N=40 3-98 months MAJOR ABDO SURGERY	24hr epidural clonidine (1mcg/ml at rate of 0.2ml/kg/hour with pre bolus of 2mcg/kg) or clonidine (1mcg/ml and ropivacaine 0.1% at rate of 0.2ml/kg/hour both got ketoprofen 2mg/kg every 8 hours breakthrough got tramadol 1mg/kg	Tramadol requirement Sedation Resp and haemodynamic changes	77% (clon) and 59.3% clon + ropiv) required no or one dose of tramadol	Sedation and decrease bp after clonidine bolus	1- no power calc
Cucchario (2003)	RCT N=26 3-12 YEARS Major GI/urology	EPIDURAL Ropivacaine 0.25% bolus (2.5 mg/kg) M (14) 0.08% Ropivacaine + 10mcg/ml morphine infusion C (12) 0.08% Ropivacaine+ 0.6mcg/ml clonidine	Pain (broadman/ VAS) Rescue Side effects	Vomiting and pruritus higher in M Pain sig higher in C group		1- power calc not based on hypothesis
Ganidagli (2003)	RCT DB N=60 Abdominal	Ramifentanil (1mcg/kg load then 0.25mcg/kg/min iv) Alfentanil (50mcg/kg load	End of anaesthesia to extubate. Verbal response	Time to extubate and time in recovery sig shorter in ramifentanil group.		1- demographics of groups different

	surgery	then 1mcg/kg/min) Combined with propofol 3 rates + mivacurium	Recovery of ventilation Orientation Time to discharge from recovery	Quality of recovery higher in ramifentanil group.		(not statistically analysed in paper)
Kiffer (2001)	RCT DB N=21 Mean age 12 Major abdominal and orthopaedic	Midaz pre med (rectal 0.3mg/kg) Epidural (n=11) 30mcg/kg bolus injection Placebo (n=10) no puncture but dressing in same spot as epidural All had PCA morphine + iv proparacetamol	Pain (VAS). Morphine consumption. Side effects.	VAS score and morphine requirements were claimed to be smaller in epidural group Opioid side effects similar in both		1- numbers required not achieved. Flawed power calc statistically flawed.
Peters (1999)	RCT N=47 5-18 YEARS Major abdo or spinal surgery	PCA (Morphine) 15mcg/kg/hour + bolus of 15mcg/kg –lock out 10min CI (Morphine) 20 to 40 mcg/kg h	Analgesia (self reporting every 3 hours via VAS) Morphine needs Side effects	Morphine consumption SIG higher in PCA No difference in pain scores	No difference in side effects	1+ Multimodal technique not used. High incidence of moderate to severe pain scores.
Chabas (1998)	RCT non blind Uro abdo surgery N=30 6-16 yrs	Epidural morphine 50ug/kg Im morphine 100uk/gh 4-5 hrly	Pain (Andersen) FVC and FEV 1 6 hours post op and every day for next 7 days	No sig difference in groups	Significant improvement in quality of analgesia and decrease morphine given in epidural group	1- no power calc
Moriarty (1997)	Prospective data collection. Non randomised N = 35	Ropivacaine (0.8 – 1.6mg/kg/4hr period) in epidurals Major abdominal and	Hourly - Pain Sedation Nausea	0.2% ropiv epidural solution inadequate alone.		3 Letter

	Ages not stated	thoracic surgery	Methods not stated.			
Kart (1996)	Prospective Descriptive Non randomised N=59 3-15 yrs	Anaesthesia and analgesia regime not standardised	Pain (Poker Chip Tool) at 1.5 hrs, 3hrs, 24 and 48 hrs post op Sedation (5 point scale) Pruritus and nausea (4 point scale)	Only 37% of children received acceptable post-operative analgesia	No best management suggested by paper	3 descriptive only
Lerman (2003)	Prospective RCT N=114 6 months – 12yrs major lower abdominal and urological surgery (hypospadias).	Epidural infusion. Lbupivacaine loading dose for all children. N=27 0.125% Lbupivcaine N=29 0.0625% Lbupivacaine N=30 1μg/ml fentanyl N=28 0.0625% Lbupivacaine and 1μg/ml fentanyl	CHEOPS every 10 mins in first hour, hourly for next 8 hrs then at 16 and 24 hrs. Proportion of children needing morphine rescue in first 10 hrs after infusion commenced.	No difference between groups for primary end point. Conclude epidural Lbupiv alone (0.0625%) is effective as a perioperative analgesic epidural solution	Sig difference in one secondary end point ($p<0.0044$ – time to first rescue dose shorter for fentanyl compared to fent and Lbupiv). Equal side effects in groups	1+.
Moriarty (1999)	Retrospective N=227 Age not stated Major abdominal, urological (small number of thoracic and orthopaedic)	Epidural infusion First 72 – 0.125% bupivacaine + diamorphine 20μg/ml Next 200 - ropivacaine solutions (0.2 – 0.6 mg/kg/hr)	5 point VAS score (faces) hourly 3 point sedation score	Lower incidence of nausea, pruritus, urinary retention and were less sedated in ropivacaine group (for comparable analgesia)		3 descriptive non randomised
Monitto (2000)	Prospective, non randomised. N=212 (240	Intravenous infusion monitored by nurse or parent (PNCA) Morphine, fentanyl or	Pain assessed by objective 6 point scale, objective 11 point scale or wong	PNCA provides effective analgesia for children under 6.	1.7% incidence of apnoea vomiting 24% pruritus 14%	3 descriptive only

	treatment episodes) Mean age 2.3 yrs Post operative pain – most common abdominal (and some painful medical conditions)	hydromorphone	baker face scale.			
Rosenberg (2005)	Prospective, non randomised N=45 Age 0-362 days (over 2.5kg) Major abdominal or thoracic surgery	Epidural infusion Bolus of 0.9 – 2.0mg/kg of ropivacaine o.2% followed by 0.2mg/kg/hr ropivacaine (infants <180 days) or 0.4mg/hr ropivacaine (infants >180 days)	Four point descriptive scale and OPS. Every 2 hours for first 8 then at 0600, 1200 and 1800 while infusion was running	Primary – evaluate pharmacokinetics Levels of unbound ropivacaine higher in neonates than infants but still below threshold levels for CNS toxicity in adults. Advised caution during first week of life.	Secondary – efficacy and safety Produced satisfactory pain relief	3 non analytical
Van Dijk (2002)	Prospective RCT N=181 Age 0-3 years Major abdominal or thoracic surgery	Continuous morphine (CM) infusion versus morphine bolus (IM) 10μg/kg/hr in fusion or 30μg/kg IM every 3 hours	COMFORT behaviour (alertness, calmness, muscle tone, movement, facial tension and respiratory response or crying). VAS (0-10) 3hrly during first 36 hours	No significant difference between groups Regimes effective for 29% of CM and 35% of IM Higher pain response in infants over 4 weeks.	No pruritus or N&V seen in any patients	1- no power calculation. Primary and secondary end points not stated. Chosen regimes ineffective (poor design)
Birmingham (2003)	Prospective Non randomised N=128 (132 procedures)	Patient controlled Epidural analgesia PCEA. Solutions include: Bupivacaine 0.1% (0.0625-	Pain by numeric rating score (0-10)and wong baker (0-5)	Showed PCEA effective in children as young as 5 with out toxicity or serious side effects	N&V 18.2% Abnormal leg neurology 17.4%	3 not analytical

	Age 5-18 Major procedures including laparotomy, orthopaedic, thoracic and urological surgery	0.125) with fentanyl 5μg/ml (2-10) was commonest solution. Ropivacaine 0.2% was also used with fentanyl 3-5μg/ml. Hydromorphone and morphine were used for one case each.	Exact frequency not stated Outcome not stated (intended to show efficacy of PCEA)		Pruritus 11.4% Urinary retention 13.3% (89% already had urinary catheters in place) 10% conversion to IV PCA.	

INTERVENTION Pyloromyotomy

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Habre (1999)	Retrospective N= 72	Wound infiltration with B (mean dose 2.16 +/-1.43 mg/kg	Timing of first post op analgesia	Paracet (mean 20mg/kg) administered after 9.12 +/-8.04 h 3 required post op opioid		3

INTERVENTION: Orthopaedics – lower limb surgery

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Hiller (2006)	DB RCT N=120 1-9 yrs (Soft tissue or orthopaedic) (11 exclusions from final analysis)	Gp1: Paracetamol 60mg/kg pr & 40mg/kg orally 8h post op Gp2: Ketoprofen 2mg/kg IV at induction & 8h post op Gp3: Both drugs	Morphine consumption OPS (0-9) for 24 h; Every 10 minutes for 2 hours, then hourly for 22 h Plasma drug concentrations at 4 hours N&V, anti-emetic use, retention pruritus	Cumulative morphine requirement less Gp3 by 30%. Difference SS Gp 1 vs Gp3 but not Gp2 vs Gp3 Mean time to 1st morphine Gp3> Gp1 & Gp2 OPS less in combination gp	Combination more effective in PACU, difference persisted in orthopaedic group for full 24 h No diff in adverse effects	1+
Goodarzi (1999)	DB RCT N=90 3-19 years (fem osteotomy, VDO, tibial osteotomy, Ilizarov & talectomy)	Comparison of epidural opiates: Morphine 10mcg/kg/h vs Fentanyl 1mcg/kg/h vs Hydromorphone 1mcg/kg/h	VAS (1-5) Side effects Hourly for 30 hrs	No difference in pain scores Resp dep: M>F=HM Somnolence: M>F=HM N&V: M>F>HM U.retention: M>F>HM	Epidural hydromorphone fewer side effects & comparable analgesic efficacy	1+

Duflo (2006)	DB,RCT N=33 7-15 yrs (large bone osteotomy, arthrotomy, cyst, tumour resection)	Fascia iliaca compartment block or sciatic nerve popliteal block. Bolus 0.2% ropivacaine, 0.5ml/kg PCRA 0.1ml/kg bolus, 30 min lockout + 0.02ml/kg/h background vs CRA 0.1ml/kg/h	VAS 4 hrly for 48 hrs Demand to delivery ratio Quality of awakening Satisfaction Plasma ropivacaine levels at 24 & 48 hrs	Mean VAS in 1st 24 h: 1.1 PCRA, 1 CRA Mean VAS in 2nd 24h: 0.8 PCRA, 0.9 CRA Supplemental analgesia: 3 PCRA, 9 CRA No diff in satisfaction or quality of awakening Ropi plasma levels: significantly lower in PCRA gp	3 exclusions Potentially lower systemic toxicity Dec cost	1+
Lovstad (2001)	DB RCT N=42	1. Sevo, epi with fentanyl vs, 2. sevo epi no fentanyl vs 3.propofol, epi no fentanyl 1: 0.1% bupivacaine, fentanyl 2mcg/ml, epinephrine 2mcg/ml 2 & 3: 0.15% bupivacaine, epinephrine 2mcg/ml	Verbal pain scale (0-4) PONV (0-3) Pruritus At 0h & 4 hrly for	Plain bupivacaine gps needed 55-75% larger bupivacaine doses & 10/26 needed IV opiates. No diff in pain scores Fentanyl: 7/16 nausea, 2/16 vomited		1+
Castillo-Zamora (2005)	DB RCT N=45 (Hip surgery)	Comparison of three doses of epidural morphine: 11.2, 15 & 20 mcg/kg	Pain Side effects	12-14 hrs analgesia in all groups	PONV: 46.7%, 60% & 86.7%, with incr morphine	1+
Bai (2004)	RCT Unblinded N=91 1-14 yrs (lower limb surgery due to CP, polio, hip dysplasia)	PCEA lidocaine 5mg/h, 2.5mg bolus, 8 min lockout vs NCA fentanyl 1mcg/kg/h background	Parent VAS & Objective Pain Score 0-10 at 0, 6 & 24 hrs Side effects	OPS lower in epi group ($p<0.05$) PVAS lower in epi group ($p<0.05$)	PONV: 16% epi group, 30% fentanyl group (not signif)	1+ (? Validity of parent VAS & OPS)
Kokki (1999)	DB RCT N=58 1-15yrs (Lower limb plus	IV ketoprofen 1mg/kg loading dose + 4mg/kg/24h vs placebo All epidural sufentanil	Rescue analgesia Pruritus, PONV	K gp 0/29 required rescue analgesia Control 8/29 rescue analgesia	No diff in PONV	1-

	urology)					
Reinoso-Barbera (2002)	DB, RCT N=30 2-16 yrs (Vertebral arthrodesis, bone graft, amputation, osteotomy)	Epidural fentanyl (1mcg/ml) + lidocaine 0.4% @ 0.1-0.35ml/kg/h vs epidural morphine 20mcg/kg 8 hrly All received IV metamizol	> 6yrs old VAS 0-10 < 6yrs old LLANTO 0-10 (validated Spanish OPS) ? frequency & duration Plasma lidocaine levels	Pain score < 4 95% of time on FL group & 87% of time in M group Statistical but not clinical significance	Plasma lidocaine levels not toxic No diff in SEs	1-
Dadure (2006)	Randomised Unblinded N=54 (club foot repair, ankle & foot osteotomy)	Continuous epidural block (CEB) vs Continuous popliteal nerve block (CPNB) Bolus 0.5 – 1ml/kg of equal volume mixture 0.25% bupivacaine & 1% lidocaine – both groups Ropivacaine 0.2% infusion at 0.1ml/kg/h for CPNB & 0.2ml/kg/h for CEB	Pain on movement VAS (0-10) or CHIPPS at 1 hr & then 6hrly for 48 hrs	No difference in pain scores or rescue analgesia Satisfaction 100% in CPNB, 86% in CEB	Increase adverse effects in CEB gp: Technical problems, urinary retention, PONV	1-
Antok (2003)	RCT Unblinded N=48 7-12 yrs (osteotomy, arthrotomy, tumour)	PCEA vs CEA 0.2% ropivacaine All received ketoprofen & propacetamol	VAS 0-10, 4 hrly For 48 hrs	No difference in VAS PCEA gp received 50% ropi dose compared with CEA gp ($p<0.001$)	No difference in SEs	1-
Tran (2005)	RCT Unblinded N=36 12-19 yrs	Fem-Sci NB with 0.125% bupivacaine & clonidine2mcg/kg (FSNB) vs intra-articular bupivacaine	VAS 0-10 at 0, 1, 4, 8, 12 ,16 & 18 hrs Intra-op fentanyl	FSNB: Dec intra-op fent ($p=0.04$) Dec morphine usage ($p=0.03$) Longer duration of analgesia	2 pts excluded from FSNB gp – failed block IA : 50% PONV	1-

	(ACL surgery)	0.25%, clonidine1mcg/kg & morphine 5mg (IA) All received PCA morphine	Morphine usage Time to 1st morphine SEs	(p=0.0001) Dec VAS (p=0.01)	FSNB: 11% PONV	
Kiffer (2001)	DB, RCT N=21 6-15 yrs	Epidural morphine 30mcg/kg vs control All received PCA morphine & IV propacetamol	VAS hrly for 24 hrs Morphine consumption Side effects	VAS & morphine requirements significantly less in epi morphine group	No difference in incidence of side effects	1+
Paut (2004)	DB RCT N=6 5-15 yrs (femoral surgery)	Fascia iliaca compartment block 0.7ml/kg 0.5% ropivacaine (4 pts) vs 0.7ml/kg 0.275% ropivacaine (2 pts)	Plasma levels of ropivacaine	3/4 pts receiving higher concentration had a Cmax that exceeded the maximum recommended level	All had satisfactory analgesia	1-
Gouda (2003)	N=36 1-=24mts (Club foot)	Comparison of IVRA with ropivacaine0.1% vs IVRA with lidocaine0.3% vs control	Time to first analgesia OPS	T to 1st analgesia = 52, 44 & 10min, ropi, lido, control		1-
Eberson (1999)	Case control N=64 6m-18 yrs (Long bone osteotomy & CTEV)	Ketorolac 1mg/kg loading dose, 0.5mg/kg 6h for 24 hrs + breakthrough IV morphine Controls (N=37) IV morphine 0.1mg/kg 3 hrly prn	Morphine usage GI complications Length of stay Bleeding complications	K gp: 2.29 morphine doses Controls 10.02 morphine doses (p<0.05)	No bleeding complications GI effects: K: 4%, controls 32% (p<0.05) Length of stay: K: 3.63 days Controls: 4.74 days	2+
Herrera (2004)	Cohort study N=35 (Femoral nailing)	Intra-operative haematoma block 1-2ml/kg of 0.5% or 0.25% bupivacaine vs control all received 0.1mg/kg morphine	"Narcotic equivalent dose" Time to 1st opiate 12 hrs	Time to 1st opiate inc by 5 hrs (p=0.08) Narcotic equivalent requirement in haematoma block gp: 0.05Eq/kg & 0.12Eq/kg at 6 & 12 hrs In controls: 0.09Eq/kg & 0.13Eq/kg (not ss)	No adverse effects	2-

Black (2003)	Retrospective Case control N=92 (Club foot surgery)	Caudal vs no caudal	Opiate usage for 8hrs	No diff		2-
Tobias (1999)	Case series N=20 6m-12 yrs (foot & ankle surgery)	Popliteal fossa block 0.75ml/kg of 0.2% ropivacaine	OPS (0-10) 30 min, 60 min& 2hrly for 12 hrs Analgesic use	12 hrs analgesia 19/20 no other analgesia for 8 hrs 8/20 no other analgesia for 12 hrs	Unsuccessful in 1 pt No adverse effects	3
Dadure (2004)	Case series N=15 1-14 yrs (Femoral shaft & hip surgery)	Continuous psoas compartment block, 0.2% ropivacaine	VAS & CHIPPS at 1, 6, 12, 18, 24, 30, 36 & 48 hrs	Median pain score 1 at 1 hr 0 thereafter	No adverse effects	3
Brenn (1998)	Case control N=92 4 – 13 yrs (CP pts, orthopaedic & Nissen fundo)	Bolus epidural morphine vs CEA bupivacaine & fentanyl		91/92 excellent analgesia	6.5% XS sedation in bolus group	3
Lejus (2001)	Prospective case series N= 348 12 days – 18 yrs (orthopaedic 80% & general)	CEA Fentanyl 0.2mcg/kg/h With Bupivacaine <20kg 5mg/kg/day 21-40kg 4.2mg/kg/day >40kg 3.2 mg/kg/day	0-5 pain score (Krane) hrly for 43 hrs Side effects	86% of all pain scores <3 2.5% pain scores = 5	PONV in 14% Pruritus 2/348 No seizures, hypotension or respiratory depression	3 Low efficacy in club foot
DeVera (2006)	Retrospective case series N=1809 2m-20 yrs	1011 lower extremity blocks 646 upper extremity blocks 579 neuraxial blocks	Complications	2 self limiting complications following PNB		3

Lovstad (1997)	Case series N=100 4-14 yrs (femoral osteotomy)	Epidural 0.1% bupivacaine, fentanyl 2mcg/ml, epinephrine 2mcg/ml Rectal paracetamol	Verbal pain score 0-4 Side effects	99% 0 or low pain score at rest for 80% of time 80% 0 or low pain score for 80% of time on movement	63% PONV 49% pruritus	3
Vas (2005)	Case series N=160 4m-12 yrs (Foot surgery, tendon transfers, tibial osteotomy)	Continuous Sciatic block 0.25% bupivacaine, 0.75ml/kg bolus followed by 0.3mg/kg/h bupivacaine	CHEOPS 6 hrly for 72 hrs	Pain score 1-4 86% 5-6 13%, 7 <1%	Block failed in 9	3
Duflo (2004)	Case series N=27 4-17 yrs (Lower limb surgery)	Patient controlled regional analgesia. Fascia iliaca block or sciatic nerve popliteal block 0.2 % ropivacaine, 0.5ml/kg bolus PCRA: 0.2% ropi 0.02ml/kg/h, 0.1ml/kg bolus, 30 min lockout Paracetamol & Ketoprofen	VAS or CHEOPS for 48 hrs Demand to delivery ratio	Mean VAS 1.09 Mean CHEOPS 4.75 2 pts req additional analgesia	2/27 motor block 1/27 catheter removed because of leak No serious complications	3
Paut (2001)	Case series N=20 1-16 yrs (Knee & thigh surgery & fractured femur)	FIC block Bolus 0.25% bupivacaine 0.62ml/kg Infusion 0.135mg/kg/h	Plasma levels at 24 & 48 hrs VAS (0-100) or CHEOPS 4 hrly for 48 hrs Block efficacy	Plasma bupivacaine levels within the safe range	No severe side effects	3
Manion (2005)	Case series N=14 5-11yrs (pelvic &	Lumbar plexus block 0.5ml/kg of 0.5% bupivacaine + 1mcg/kg clonidine	Pain score? which For 72 hrs	Effective analgesia	No complications	3

	femoral surgery)					

INTERVENTION: Upper limb surgery (Orthopaedic & Plastic surgery)

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Iwata (2000)	DB, RCT N=26 2-11 years	Fentanyl brachial plexus block vs saline Axillary approach	Time to onset of pain	Time to onset of pain in fentanyl group 809 minutes, 199 in controls		1-
Thornton (2003)	DB, RCT N=35	Axillary block with 0.2% ropivacaine 0.5ml/kg vs 0.25% bupivacaine 0.5ml/kg	FLACC at 0,3,6,12 & 24hrs Time to 1st opioid analgesia	No difference		1+
Fleischmann (2003)	Prospective, randomised N=40 1-10 years	Axillary (ABP) vs Lateral infraclavicular (LVIBP) Both groups: 0.5ml/kg of 0.5% ropivacaine	Sensory & Motor blockade	Sensory (quality & distribution) & motor blockade more effective in LVIBP	No major complications in either group LVIBP less painful	1-
Pande (2000)	Prospective case series N=200 5-12 years	Supraclavicular brachial plexus block for upper extremity trauma	Ability to perform procedure	Satisfactory block	No pneumothorax	3
Carre (2000)	DB, RCT N=70 4-15 years	Single injection (S) vs multiple fractionated doses (M) for axillary block	Motor & sensory block	No benefit to fractionated doses (easier diffusion of LA in perineural space cf adults)		1+
Fisher (1999)	N= 185 patients, 250 procedures Case series 5 mts – 17 yrs	Axillary block with 0.25% bupivacaine 0.5-0.6ml/kg	Intra-operative & postop analgesia	54% no further intra-operative analgesia Block failed in 6%	No complications	3
De Jose Maria (2004)	Case series N=55 5-17 yrs	Vertical infraclavicular block with 0.5ml/kg of 0.5% ropivacaine	Number of attempts, response to surgery, VAS,	1st or 2nd attempt 85% 3rd or 4th attempt15% 98% effective for surgery VAS <3 all patients	No pneumothorax or puncture of major vessel 2 pts Horner's	3

			complication & duration of block	Mean sensory block 8.45 hrs Mean motor block 6.52 hrs		
Altintas (2000)	N=49 1-11 yrs	Axillary block with 0.8ml/kg of 0.25% bupivacaine Performed pre-surgery or post surgery	Isoflurane requirements Faces 2, 4, 6, 8, 10 & 24 hrs Analgesic requirements for 24 hrs	No difference in pain scores in 1st 8 hours. 8 in pre-group & 20 in post group did not require analgesia in the 24 hr study period		1+

INTERVENTION: Spinal Surgery

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Gall (2001)	DB, RCT N=30 9-19yrs	All: PCA morphine Intrathecal morphine 0, 2 or 5 mcg/kg	Time to 1st morphine Morphine consumption VAS (0-100) at rest & on movement For 24 hours	Time to 1st morphine: 5>2>0 mcg/kg VAS at rest: 5=2>0 mcg/kg VAS on movement no difference	Dec intra-op bleeding with 5mcg/kg	1+
Munro (2002)	DB RCT N= 35 11-17yrs	IV ketorolac 0.5mg/kg 6h for 36h post-op All: PCA morphine	Pain & sedation assessed bd for 3 days, morphine consumption, pruritus, nausea, constipation	K group lower pain scores 1st & 2nd days ($p<0.05$), dec morphine consumption No diff in morphine related adverse effects	No diff in bleeding No failure of fusion at long term follow up	1+
O'Hara (2004)	DB, RCT N=31	All: PCA morphine Epidural: bupivacaine: 0, 0.1% or 0.0625% Both bupivacaine solutions contained 5mcg/ml fentanyl (mid-thoracic epidural)	VAS, morphine usage, 4 hourly for 96 hours Time to oral intake, ambulation & discharge	No difference		1+
Blumenthal (2006)	RCT N=30 11-17yrs (Anterior surgery)	Double epidural catheter 0.3% ropivacaine(E) vs Continuous IV morphine 50mcg/kg/h (M) (All received TCI remi until 1st post-op morning = T0)	VAS(0-100) at rest (6hrly) & on movement (24, 48 & 72h) Rescue analgesia	E group: significantly less pain at rest & on movement, less rescue morphine, improved bowel activity & higher patient satisfaction	Motor block – transient in 2 patients. No hypotension Less PONV & pruritus	1+

		All received rofecoxib & IV paracetamol	Motor block PONV & pruritus (6 hrly), Bowel function (12hrly) Patient satisfaction		No neurologic complications	
Blumenthal (2005)	Prospective, randomised, unblinded N=30 12-22yrs	Continuous IV morphine vs double epidural catheters 0.3% ropivacaine (All received TCI remi until 1st post-op morning = T0)	VAS (0-100) at rest & on movement Rescue analgesia PONV, pruritus 6 hrly from T0 – T72h, bowel function 12 hrly	Epi group: VAS lower at rest except at 12, 60 & 72 hours. VAS lower on movement at 24, 48 & 72 hours	Epi group: Less pruritus & PONV Bowel function better	1-
Cassady (2000)	Prospective, RCT, unblinded N=33 11-18yrs	Thoracic epidural bupivacaine + fentanyl vs PCA morphine	VAS, time to resumption of bowel sounds, liquid intake, and side effects	No difference in pain score	Earlier resumption of bowel sounds in epi group – but no diff in time to oral intake	1-
Goodarzi (1998)	Prospective Randomised 10-16y N=80	Intrathecal morphine 20mcg/kg + 50mcg sufentanil vs IV sufentanil	"descriptive scale" 0-10	IT group "pain relief for 14.5hrs" IV group required PCA morphine	IT group decreased blood loss IT group: respiratory depression in 1st hour but not thereafter	1- No mention of pain scores in results
Sucato (2005)	Retrospective Case Series N=613	Epidural 0.1% bupivacaine + hydromorphone vs PCA morphine	Faces (0-5) At 2,4, 6, 8,12, 24, 36 & 48h	Epidural group had significantly better pain scores on average & at each time point. Range of pain scores & average max score less in the	Epi group had inc pruritus, PONV & respiratory depression	2++

				epi group		
Vitale (2003)	Retrospective review of complications of ketorolac use N=208	Ketorolac (60 pts) vs no NSAID (148 pts)	Post-op bleeding & bone fusion	No difference		2+
LaMontagne (2003)	RCT Unblinded 11-14 yrs	Coping instruction vs concrete objective information vs combination All had PCA	VAS 0-10 Day 2-4	Coping strategy gp reported less pain		2
Shaw (1996)	Case series N=71 (30 retrospective & 41 prospective) 7-19 yrs	Epidural 0.0625% - 0.125% bupivacaine with fentanyl, morphine or hydromorphone (61pts)		Did not compromise neurological assessment 64 effective analgesia		3
Lowry (2001)	Prospective review N=10 (anterior fusion)	Epidural fentanyl 1mcg/kg + hydromorphone 5 mcg/kg at end of surgery. Post-op 0.1% ropivacaine + hydromorphone 10mcg/ml @ 0.2ml/kg/h	VAS 0-10 For 5 days	Mean of median pain scores: 2.1 Mean maximum pain score: 4.1	3/10 pruritus 1/10 drowsiness	3
Tobias (2001)	Case series N=14 5-17 yrs	Double epidural Fentanyl + hydromorphone at end of surgery Post-op ropivacaine + hydromorphone	VAS 0-10 & objective pain score 0-10. 2-4hrly for 5 days	Mean of median pain score: 1.5, 1.6, 1.4, 1.1, 0.9 Mean of maximum pain score: 3.5, 4, 3.1,2.4, 2.2.	No adverse effects	3
Ekatodramis (2002)	Prospective case series N=23 12-19 yrs Anterior surgery	Double epidural 0.0625% bupivacaine, fentanyl 2mcg/ml & clonidine 3mcg/ml	VAS 6 hrly for 48 hrs	VAS 0 at rest in all patients VAS 30 on movement in 17%	Pruritus 0 N&V 17%	3
Turner (2000)	Case series N=14	Epidural bupivacaine 0.1% bupivacaine + 5mcg/ml fentanyl	VAS Placement checked radiologically	Correct placement associated with “effective analgesia”		3

Arms (1998)	Case series N=12 10-18yrs	Epidural 0.0625% - 0.125% bupivacaine + morphine	Faces 0-10	Effective analgesia	Pruritus 7/12	3
Goodarzi (1996)	Case series N=10 15-18yrs	IT morphine 20mcg/kg + 50mcg/kg sufentanil	Effect on SSEPs	No effect on SSEPs		3

INTERVENTION: Plastic surgery of head and neck (Cleft lip & palate & otoplasty)

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Bremerich (2001)	DB RCT N=80 1-20 months Cleft palate	Rectal paracetamol: 10, 20 & 40mg/kg vs placebo	Paracetamol plasma level CHIPPS (0-10) Opioid administration	Plasma levels sub therapeutic No difference in opioid use		1+
Prabhu (1999)	DB RCT N=30 4-20 months Cleft lip	Infra-orbital nerve block vs peri-incisional local infiltration 0.125% bupivacaine	Pain **relief** score (Attia) 0-20 At 0,1,2,4, 8 & 24 hrs	Statistically significant better pain relief up to 8 hrs post-op with IOB. IOB less rescue analgesia	Not recorded	1+
Cregg (1996)	Single blind randomised N=43 3-15 yrs Otoplasty	Gp A local infiltration with 1% lidocaine with epi 0.4ml/kg Gp B regional nerve blockade with bupivacaine 0.5% 0.4ml/kg	Pain score (0-10) At 0, 30,60,90,120,180, 240, 360 & 480 min Time to 1st supplemental analgesia	No differences in pain scores, supplemental analgesia or PONV Time to 1st supplemental analgesia 8.6h gp A, 10.5 gp B	Haemostasis better in lidocaine with epi gp	1-
Dawson (1996)	Single blind, randomised N=34 Mean age 11 yrs Alveolar cleft bone graft	All received PCA morphine 0.015mg/kg 8 min lockout 18 received ketorolac 1mg/kg loading dose followed by 0.5mg/kg 6h	Morphine usage Time to mobilisation & discharge	No difference in morphine usage No difference in time to mobilisation or discharge	Effect on bleeding not studied	1-
Eipe (2006)	Case series N=20 Cleft lip	Infra-orbital nerve block	Time to 1st analgesia	6-24 hrs analgesia		3

Sylaidis (1998)	Case series N=20 6m-9y Cleft palate	Diclofenac 1mg/kg 12 hrly & Paracetamol	Risk of post-op haemorrhage	Effective analgesia No further opiates required	Early discharge Not associated with increased bleeding	3

.

INTERVENTION: Neurosurgery

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Tobias (1997)	Case control n=24 13m-10.5 yr	Intrathecal morphine 20mcg/kg vs No treatment (retrospective cohort)	Time to first postoperative analgesia Total dose paracetamol and Nalbuphine 24hr VAS (>5yr) or Unvalidated behavioural scale	Significant delay in TTA (p,0.0001) Significant reduction in total doses postoperative analgesia Scores not reported	PONV, pruritis, urinary retention, respiratory depression (no difference)	2-
Monitto, (2000)	Case series n=240 Mixed cases 0-6 yr (2.3±1.7 sd) 12 neurosurgery	Parent/ Nurse controlled analgesia with fentanyl (10 cases) or hydopmorphone (2 cases)	Duration of treatment Daily morphine dose Max daily pain scores ('objective pain score' or self report)	Duration of treatment 4 (3-5) days. Neurosurgery patients 4 (3-5). Morphine use ± 30mcg.kg.hr on ist 2 days decreasing thereafter. At least 80% pain scores, 3/10 on 1st 2 days.	Naloxone for resp. depression 9/250 No significant risk factor (including age) identified.	3
McEwan et al. (2000)	RCT (?blinding) Pharmacokinetic study	IM or rectal Codeine Phosphate 1mg/kg	CHEOPS	No difference in analgesia (CHEOPS scores all high!)	No difference in absorption or peak plasma levels	1-

INTERVENTION: Cardiac surgery/ sternotomy

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Finkel et al., (2002)	RCT not blind 14, 2x7 7mths-7.5 yrs	Intrathecal Morphine 10mcg/kg + hyperbaric tetracacine 0.5% or tretracaine followed by Hypobaric Morphine/saline	Pain score Duration of analgesia 1hrly/12hrs	No difference in scores/duration	PONV decreased in hypobaric group	1- small size unblinded
Pirat et al., (2002)	RCT 30, 3*10 6months-6years	IV fentanyl IT fentanyl IV+IT fentanyl	COMFORT CHEOPS Analgesia in CICU Cortisol Glucose, insulin ,lactate 24hrs.	No difference in pain scores or Time to 1st analgesia	PONV Time to extubation(TTE) No diff PONV TTE IT+IV<IT=IV	1- Small size Randomisation not described Blinding'observer unaware'
Gupta et al., (2004)	RCT 70, 2x35 2.5months-14.5ys	IV ketorolac 0.5mg/kg (max 15mg) Commenced 6 hours after admission to CICU. Sig. bleeding in 1st 6 hrs excluded	Bleeding 48hrs	No difference, ketorolac didn't increase bleeding	TTE, Morphine requirement, pericardial effusion. Length of hospitalisation Creatinine. No difference	1+ no pain scores, no difference in analgesic requirements.
Suominen et al., (2004)	RCT 71, 35+36	IT Morphine 20mcg/kg vs Intravenous morphine	Analgesic consumption. Time to 1st analgesia. (TTFA) 24hrs	Morphine consumption (0.03) TTFA 8.7 vs 12.3hrs (0.003)	PONV Itching Respiratory Depression No difference	1+ Closed envelope randomisation. IT group significantly

					0.65	younger.
Hammer et al., (2005)	RCT 37, 17+18 3months-6years	IT Tetracaine0.5% +Morphine 7mck/kg vs No treatment Remi-based GA technique	Pain score FLACC/Wong Baker Analgesic consumption-PCA fentanyl 5+ days	Pain scores lower in IT group for 8 (0.046) and 24(0.05) hours. Fentanyl consumption lower at 8(0.003) and 24(0.004) hours.	Vomiting Respiratory depression Itching All no difference.	1- Randomisation not described Observer blinded
Chu (2006)	RCT 40 3.5yrs (±2.5)	IV Tramadol vs IV morphine NCA	CHEOPS Sedation scote TT Awakening TT1st NCA bolus TTTExtubation Vital signs	No difference in pain score Time to awakening shorter with tramadol	PONV Resp depression ICU stay No difference	
Shayevitz et al.,(1996)	Case control (retrospective casenote review) 54, 27=27 5-6 years old (0.3-19)	IV opioid, IVO, Fentanyl (6 mcg/kg/min) vs Lumbar epidural morphine LEM (3-4 mcg/kg/min)	'Global pain rating' using observer VAS Supp opioid medication Time to extubation Transfer from ICU Resumption normal diet. Discharge LOS. 5 +days	"Global pain rating" less day 1 for LEM Supplementary analgesic use less for late extubated LEM No differences for non-pain outcomes in early extubated. Shorter ICU stay, time to normal diet for late extubated	PONV Itch No difference	2- ~47 sets of records examined in each group and 27 selected according to pre-set criteria. Use of 'opioid equivalents' LEM may be useful for selected populations.
Leyvi et al., (2005)	Rectrospective cohort study 3 cohorts ASD 34, VSD 37,	Caudal Morphine 70-110mcg/kg + Bupiv 0.25% 1ml/kg vs IV Opioid	PICU/ hospital stay	No differences detected	FLACC and Morphine consumption in mixed subgroup	2- risk of bias, small number in pain analysis

	TOF 46				(25 pts). No difference	
Hammer et al.(2000)	Retrospective case series. 50, 25 SAB and 25 TEB Ages ~3-5ys	SAB tetracaine + Morphine TEB bupivacaine 1.25mg/kg+ hydromorphone	Vital signs Hypercarbia PONV Wong-Baker (>3yr) Unspecified behavioural pain scale (<3yr)	Vital signs, no difference. SAB more Analgesia and sedation than TEB. PONV no difference but SAB received prophylactic ondansetron.		3 (9 cases also in Petersen et al 2000)
Petersen et al. (2000)	Retrospective case series. 220 (76 non-sternotomy)	SAB Tetracaine +Morphine TEB Bupivacaine or Lidocaine+ Morphine or hydromorphone Caudal Bupivacaine + morphine	OPS (<3yr) Wong Baker (>3yr) VAS>7yr Analgesia requirement	TEB Pain score <5 for 48hr in patients with catheters 51/55 No cath, variable time to 1st analgesia 7-13hrs.	PONV 86/220 Itching 21/220 Urinary Retention 16/220 (most catheterised!) Resp depress 4/220 Infection 0 Haematoma 0	3 (9 cases also in Hammer et al 2000)

INTERVENTION: Thoracotomy

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Bozkurt (2004)	RCT (not blind) Ages 2-14 yrs n=32 (16 x2)	Thoracic epidural morphine 100mcg/k vs IV morphine infusion 20mck/kg/hr (LD 50mcg/kg)	Pain (24hr; 1, 4, 8, 12, 24 (Wong Faces) Sedation Compications Plasma Cortisol Plasma Glucose Insulin Se Morphine	Pain scores similar at 1 4 8 12 hrs Epi>systemic 24hr Rescue 5/16 epi 1/16 IV morphine Conclusion no difference	Sedation no diff PONV Epi4/16 IV 2/16	1- I think that IV is superior.
Matsota (2001)	RCT Ages 5-12 n=20 (2x10)	Direct vision Intercostal Bupivacaine (3mg/kg) vs IV single dose pethidine (1mg/kg)	Duration (time to first analgesia) Side effects	Longer duration with ICB	No side effects	1-
Lynn (2003)	Cohort study. Comparison of cyanotic and acyanotic infants n=20 (2x10) 0-90 days	Continuous infusion of morphine to target plasma concentration of 30ng/ml	Modified infant pain scale	Effective analgesia in both groups	Age more important than presence of cyanosis for morphine clearance CO2 response curves similar in both groups	2- ?validity of pain score
Lynn (2000)	RCT Infants 42-165 days N=83 Mixed surgery, 5 thoracotomy	Continuous or intermittent (bolus) morphine All received paracetamol	Modified infant pain scale	Infusion more effective at reducing pain scores ($p<0.001$) but higher dose with infusion.		1- low number of thoracotomy patients limits transferability of findings ?validity of pain score

van Dijk (2002)	DB RCT Comparison of IV infusion and bolus N=181 (30 thoracotomy) Ages 0+3years	Efficacy of 10mcg/kg CI vs 30mck/kg bolus 3 hourly. Following 100mcg/kg loading dose.	COMFORT VAS	60% if patients in both groups effective analgesia. Age and dose related differences. 10mcg/kg ineffective in 30% of patients. This dose more effective in neonates.		1- not stated which groups thoracotomy patients distributed.
Cheung (1997)	Prospective observational study/ case series. Ages: 1.5 weeks Range 0.1-20.4 Newborn to 5 months n=22	Continuous Paravertebral Direct vision catheter placement after surgery. GA with Fentanyl 2mcg/kg. 1.25mg/kg bupivacaine + Epi LD, followed by 0.25mg/kg/hr (fixed rate) All patients received paracetamol	CRIES pain score for 48hr (modified) 'Rescue' IV morophine Serum bupivacaine	18/22 median mean pain score 0.29 (0.00-1.63) 86% satisfactory analgesia. 3 patents rescue morphine. Serum bupivacaine > 3mcg/ml in 3 patients (30, 42, 48hr) No observed toxicity	2/22 leakage of infusate 2/22 accidental disconnection	3 No formal measurement of clinical toxicity
Downs (1997)	Prospective observational study/ case series Ages 1-9 years n=9	Exprapleural Intercostal block (/ paravertebral), direct vision. Bupivacaine LD 0.25-0.5% 0.28±0.1ml/kg) , infusion 0.21±0.09ml/kg/hr Bupivacaine infusion 72±15hr Morphine infusion 48hr	Bupivacaine dose Posoperative morphine requirements (continuous infusion or PCA)	Mean dose bupivaciane 0.28±0.08 mg/kg/hr Morphine < 0.03mg/kg/hr	No PONV No Resp depression	3 Abstract only
Gibson (1999)	Retrospective case control. Ant. spinal fusions and thoracic surgery n=13	Retropleural intercostal catheter Bupivacaine 0.25-0.125% at 0.5ml/hr (n=7)+ IV morphine IV morphine only controls (n=6)	Total morphine use	Morphine 0.544mg/kg/day vs 0.204mg/kg/day P=0.001		2- no pain scores or discussion of quality of analgesia
Higgins	Retrospective	Administration of prescribed	Total drugs	Thoracotomy patients < 24		3

(1999)	Audit/ Case series Strenotomy and Thoracotomy patients n=114	regular analgesia Use of faces pain scale in older than 39 months	administered Frequency of pain evaluation	months old least analgesia Sternotomy patients .36 months most analgesia Pre-dose Scale 35%, post dose 15% Conclusion: analgesia poorly managed		
Karmakar (1996)	Case series Infants 5.3weeks (2d-5months) n=20	Paravertebral block Bupivacaine 1.25mg/kg LD followed by 0.5mg/kg/hr	CRIES Rescue morphine infusion Serum bupivacaine 24hr.	18/20 (90%) pain score 0.46 (0.0-1.4) Maximum bupivacaine 2.0 cg/ml (SD 0.63).	1 Patient ipsilateral Horners syndrome.	3
Semsroth (1996)	Case series n=20 9 infants < 15kg 11 children >15kg	Intrapleural bupivacaine LD 0.625mg/kg+Epi, followed by 1.25mg/kg/hr	Pain Score Infusion rate adjustment Supplementary opioid	Intrapleural bupvacaine is effective for infants and children	No Cardiorespiratory complications	3 Abstract only
Shah (1997)	Case series Age 9.8yrs (2-16) n=15	Paravertebral block 9 Pre-emptive 6 Postoperative	Faces Pain Score VAS Rescue morphine requirements	No differences in alalgesia Paravertebral block is effective	No complicationswolf	3 Abstract only
Ioscovich, (2004)	Case series 10-15years old	Intrathecal morphine 80-100microgm in 2ml saline.	VAS 2hrly Sedation score	VAS <3 No additional opioids in 1st	PONV 1/7	3

	n=7 (6 thoracotomy, 1 sternotomy)	All patients received IV paracetamol 1-2 g or dypirone 500mg 6hrly	Rescue analgesia 24hrs	24hrs		
Kokki (2006)	Case series 10m-12yrs n=10	Interpleural bupivacaine +epi 2mg/kg, then 1mg/kg 2hrly for pin score > 4 IV oxycodone 0.1mg/kg if pain score not reduced by bupivacine All received 10mg/kg rectal Ibuprofen 6hrly	Pain score: VAS Total bupivaciane doses Total oxycodone doses	All received 3-10 (6.1 SD 2.3) doses bupivacaine. All children received 3-10 doses oxycodone (6 SD 3.6)	Interpleural bupivacaine = ibuprofen isufficient for thoracotomy pain	3
Lin (1999)	Retrospective case series 7months-27months N=27	1. Single injection caudal bupivacaine 1mg/kg + epi (n=6) 2. Single injection caudal bupivacaine 1mg/kg+epi, +PF Morphine 50-100microgm/kg (n=11) 3. LD Bupiv 0.5-0.75mg/kg+PF Morphine 10+30microgm/kg then 0.1%bupivacaine+morphine 10microgm/ml at 0.25-0.3ml/kg/hr (n=10)	Supplementary postoperative opioid	Continuous infusion (Gp3) no postoperative opioid supplements (p=<0.05)	Duration of anaesthesia Gp3>Gp2 (p0.05) Length of ICU stay: Gp 3 , Gp2 (p<0.05) POEmesis: Gp 2> Gp 3 (p=0.05) Time to oral intake Gp3<Gp2 (p<0.05) Length of hospital stay Gp3 < Gp1 (p<0.05)	2- Unvalidated pain score (0-10)
Karmakar (1997)	Case report N=1 11 months old	Bilateral paravertebral catheters	Pain score Supplementary analgesia Serum	Satisfactory pain scores No supplementary analgesia Bupivacaine levels below toxic.		3

			Bupivacaine			
Birmingham, (2003)	Case series	PCEA				3
Monitto, (2000)	Case series n=240 Mixed cases 74 abdominal surgery	Parent/Nurse NCA				
Lejus (2001)	Prospective evaluation of epidural over 6 years. n=348 (307 children 12 days to 18 years, median 72 months)	Bupivacaine (mean concentration 0.185%)and Fentanyl (5ug/kg/day). Different types of surgery including fundoplication (9).	Hourly pain scores (Krane et al) Global pain index	Combination provides safe/ effective analgesia	Urinary retention 17% N & V 14% Pruritus 0.6%	3 prospective but not analytical
Peters (1999)	RCT n=47 5-18 YEARS Major abdo or spinal surgery	PCA (Morphine) 15mcg/kg/hour + bolus of 15mcg/kg –lock out 10min CI (Morphine) 20 to 40 mcg/kg h	Analgesia (self reporting every 3 hours via VAS) Morphine needs Side effects	Morphine consumption SIG higher in PCA No difference in pain scores	No difference in side effects	1+ Multimodal technique not used. High incidence of moderate to severe pain scores.
Moriarty (1999)	Case series/ unmatched cohort study n=272 (n=29 thoracic)	72 children received an infusion of bupivacaine 0.125% + diamorphine 20 microg x ml-1, then 200 children received plain ropivacaine solutions. PRN diclofenac (or codeine)+ paracetamol.	Pain score (‘5 point faces score’ validity not stated) Sedation score ‘Nausea score’ Pruritis	Both methods satisfactory analgesia (±20%incidence of moderate pain: pain scores < 3).	Difference in side effects for PONV and pruritis (significance not reported)	3 Thoracic sub-group not specifically identified/reported